Inventory of Projects

DRAFT Wednesday June 05, 2002

Progress Report: Implementation of

A Public Health Action Plan To Combat Antimicrobial Resistance (Part I: Domestic Issues)

June 2002

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Focus Area I: Surveillance			
Action Item #1: Determine Which Organisms and Susceptibility to Specific Antimicrobial Drugs Should Be under Surveillance and Create a Mechanism for Periodic Updating of This List.			
CDC, USDA, FDA, DoD, DVA	Public Health Surveillance	Organisms currently under public health surveillance for antimicrobial resistance include: Campylobacter, *E. coli* O157:H7, Gram negative and gram positive organisms causing health care associated infections, group A *Streptococcus,* group B *Streptococcus, Haemophilus influenzae, Helicobacter pylori,* HIV, Influenza, Malaria, *Mycobacterium tuberculosis, Neisseria gonorrhoeae, Neisseria meningitidis , Pneumocystis carinii,* Salmonella, Shigella, *Staphylococcus aureus, Streptococcus pneumoniae, Streptococcus pyogenes,* and *Trichomonas vaginalis.* Organisms are added to this list when resistance emerges as a public health problem, as tools are developed for detecting resistance, and when there is capacity at the appropriate level.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
****TOP PRIORITY**** **Action Item #2: With Partners, Design and Implement a National AR Surveillance Plan.**			
CDC	Council of State and Territorial Epidemiologists (CSTE)-Association of Public Health Laboratories (APHL)-CDC working group	Working group to develop strategies for AR surveillance through improved state health department epidemiology and laboratory capacity and reviewing methods for antimicrobial resistance surveillance for different pathogens of public health importance to be used at state and local levels for support prevention and control activities.	Ongoing.
CDC	Enhanced collection and electronic transfer of data on Antimicrobial Use and Resistance (AUR)	A cooperative study of enhanced collection, compilation, and transmission of data on antimicrobial use and resistance fro automated laboratory instrumentation systems in healthcare settings to CDC and other public health systems using architecture fully compatible with National Electronic Diseases Surveillance System (NEDSS). This will create a database that will facilitate benchmarking and performance feedback to promote local AR improvement efforts, development of regional, state, and national data about patterns of use and resistance; and evaluation of prevention programs.	Ongoing. During FY 2001, collaboration was established with bioMerieux Inc., and funding was allocated. Specifications for reporting electronic AUR data will be developed in FY 2002 and bioMerieux will modify their "Theratrac 2" instrument to incorporate the exportation and reporting of electronic messages containing AUR data.
CDC	Including antimicrobial resistance surveillance in electronic laboratory-based reporting activities in the National Electronic Disease Surveillance System (NEDSS)	Develop, demonstrate, and then implement automated, electronic reporting of susceptibility findings to health departments by using nationally-recognized data transmissio and coding standards and sending the data through CDC's secure data network. The result of this project will enable various other AR surveillance activities to be used for this electronic communications medium.	Ongoing.

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CDC	Active Bacterial Core Surveillance (ABCs)	At 9 Emerging Infections Program sites (EIPs), surveillance is conducted for invasive bacterial diseases due to pathogens of public health importance. For each case of invasive disease in the study population, a case report with basic demographic information is filed and, in most cases, bacterial isolates from a normally sterile site from patients are sent to CDC for laboratory study. System tracks emerging antimicrobial resistance in isolates of *Streptococcus pneumoniae* and *Neisseria meningitidis*. Data provide an infrastructure for further research, such as special studies aimed at identifying risk factors for disease, postlicensure evaluation of vaccine efficacy, and monitoring effectiveness prevention policies.	Ongoing.
CDC	Translating lessons learned from ABCs to guide surveillance for drug-resistant *Streptococcus pneumoniae* (DRSP) in local and state health departments	A series of activities aimed at translating the lessons learned from ABCs for implementation in local and state health departments where information on DRSP is needed, but resources are limited and the goals of surveillance are more local in scope. A group of epidemiologists, microbiologists, and state health department personnel will develop a draft background document, then convene the DRSP working group to draft recommendations for surveillance at state and local health departments; this meeting would include representatives from sites planning to do local or state surveillance, as well as national, state, and local public health representatives and DRSP authorities.	Ongoing. Convened panel of experts to provide input to CDC on perceived needs and goals of local and state health departments for DRSP surveillance, conducted informal need assessment to help shape direction of materials development for guidance for DRSP surveillance and uses of data, hired DRSP coordinator, and provided program funds to selected states for DRSP surveillance activities.

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CDC	National Healthcare Safety Network (NHSN)	The NHSN will be an Internet-based nationwide network that will monitor trends in adverse events associated with invasive devices, procedures, and medications used in the delivery of healthcare. Under the NHSN's Medication-associated Adverse Event Module, initial focus will be on use and resistance of antimicrobial agents and on establishing electronic reporting of antimicrobial use and resistance data to increase efficiency, timeliness, and accuracy of the monitoring effort. When implemented, the NHSN will significantly enhance the ability to monitor and track trends of usage and resistance of microbes to antimicrobial agents in a variety of healthcare delivery settings. These data can then be used to enhance patient safety by enabling healthcare workers to develop and deploy strategies to prevent overuse and inappropriate use of these agents, as well as strategies to prevent other pathogens from becoming resistant.	Initiated. In FY 2001, started software development, held joint application development session with current and potential users, and started work on data model, security, standard nomenclature for pathogens and antimicrobial agents, and user interface.
CDC	The National Nosocomial Infections Surveillance (NNIS) System	A cooperative effort between the CDC and >300 hospitals to create a national nosocomial infections database. The database is used to reveal the epidemiology of nosocomial infections and show antimicrobial resistance trends, among other purposes.	Ongoing. The data from the NNIS System are reported annually in the NNIS Report which appears on the NNIS Web page (http://www.cdc.gov/ncidod/hip/SURVEILL/NNIS.HTM) and in the November-December issue of the *American Journal of Infection Control*.

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CDC, FDA, NIH, USDA	Expand and enhance of the National Antimicrobial Resistance Monitoring System (NARMS) for enteric bacteria	NARMS is a collaboration among CDC, U.S. Food and Drug Administration (Center for Veterinary Medicine) and U.S. Department of Agriculture (Food Safety and Inspection Service and Agricultural Research Services). State health departments send *Salmonella, Shigella, Campylobacter* and *E. coli* O157:H7 isolates received at their public health laboratories to CDC for susceptibility testing. In FY 2001, NARMS launched the "Retail Food Study." Five participating states purchase ground beef, pork, ground turkey, and chickens from grocery stores and test them for enteric bacteria. Through NARMS, CDC provided support to the Michigan Department of Health for a program on appropriate use of antimicrobial agents in agriculture. This will foster collaboration between the state public health department and state agriculture (veterinary diagnostic) laboratories. CDC is helping develop a community-based program on appropriate use of antimicrobial drugs in animals. A model veterinary school curriculum for appropriate use will be developed, in partnership with FDA and the American Veterinary Medical A	Ongoing. Plans are to expand NARMS to all 50 states, providing national surveillance for antimicrobial resistance among foodborne pathogens. The number of participating states increased in 2001 to 27, and the population under surveillance increased to 63% of the U.S. residents.
CDC, DoD	Gonococcal Isolate Surveillance Project (GISP)	Sentinel surveillance system for monitoring AR of *Neisseria gonorrhoeae* in the United States established in 1986. Male urethral gonococcal isolates together with clinical and demographic patient data, are submitted for susceptibility testing each month from STD clinics in approximately 26 cities in the United States. Monitored U.S. trends in AR for *N. gonorrhoeae*. GISP data demonstrate the ongoing sprea of fluoroquinolone-resistance and the emergence of *N. gonorrhoeae* with decreased susceptibility to azithromycin in the U.S. GISP data have been regularly reported to clinician and DoD participating sites in the *Morbidity and Mortality Weekly Report*.	Ongoing. GISP data were used to revise CDC's *Guidelines for Treatment of Sexually Transmitted Diseases* in 2002. GISP data from 2000 and from previous years are available on the internet (http://www.cdc.gov/std/gisp2000/). Data from 2001 will be available by Fall 2002. Recruitment of additional DoD sites continues.

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CDC	Surveillance projects of HIV antiretroviral drug resistance	Surveillance for HIV antiretroviral drug resistance among different populations (adult, adolescent, and pediatric) and geographic areas in the U.S. using different methodologies, including phenotypic and genotypic testing. Determine transmission of drug-resistant strains to previously uninfecte persons and from mother to infant. When data are available, will support experts in deliberating potential recommendation for antiretroviral resistance testing before treating drug-naïve new patients. Will support prevention projects in evaluating success of risk prevention measures directed towards HIV-seropositive patients in treatment.	Ongoing. Funds awarded to participating state and local health departments.
CDC	National Tuberculosis Surveillance System (NTSS)	Ongoing collection, analysis, and communication of national tuberculosis surveillance information; expanded in 1993 to include the frequency and type of AR, enabling strategically focused tuberculosis control and elimination efforts. The expanded national TB surveillance system has proven its usefulness in assisting in the evaluation of the success of TB control efforts and monitoring the status of the epidemic, particularly through the collection of data on initial drug susceptibility. Information on the use of initial regimens of 4 first-line drugs, directly observed therapy, and completion of therapy in 1 year or less have been used as measures to evaluate program success. As future efforts towards TB elimination increase, both existing and new surveillance systems at the national, state, and local levels will become even more critical to monitor the burden and impact of TB, evaluate the success of control and prevention efforts, and direct planning and policy development.	Ongoing. Publications and recommendations based on these data available on the internet (http://www.cdc.gov/nchstp/tb/pubs/pem.htm).

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CDC	Nationwide estimate of the prevalence of methicillin-resistant *Staphylococcus aureus* (MRSA) nasal carriage, using the National Health and Nutrition Examination Survey (NHANES) US population-based sample	MRSA infections have been increasingly reported in the community. This project will use NHANES to measure the prevalence of MRSA nasal carriage in the U.S. population, describe the demographic and behavioral factors associated with MRSA nasal carriage, create a population-based nation MRSA isolate library, including susceptibility and molecular typing patterns, estimate the national burden of individuals at risk of developing community MRSA-associated adverse outcomes (e.g., infection), and analyze trends in emergence of resistance. Information concerning the burden of MRSA carriage in the U.S. population will help set priorities concerning allocation of public health resources for surveillance activities at the national, state, and local level ar for future national objectives and prevention programs.	Ongoing. In 2001, the project began enrolling patients, collecting data, and acquiring swabs.
CDC	The epidemiology ofMRSA strains in the U.S., using PulseNet	PulseNet is an innovative, laboratory-based national surveillance program that tracks the pulsed-field gel electrophoresis (PFGE) profiles of selected bacteria. In collaboration with state health departments, MRSA strain types and their AR profiles in the U.S. are monitored through PulseNet to determine similarity with MRSA strains throughout the country, the prevalence of MRSA strain types from which vancomycin-intermediate strains of MRSA are derived, and similarity of U.S. epidemic strains of MRSA to those known to cause outbreaks and epidemics in Europe, Canada, and the Far East.	Ongoing. Data from this nationwide system have already bee used to begin to understand the spread of specific MRSA strains among certain groups of patients in hospitals and in th community and will provide a clearer picture of the pathogenicity of*S. aureus* and the spread of AR among staphylococci.

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CDC	Surveillance for Emerging Antimicrobial Resistance Connected to Healthcare (SEARCH)	Normally, vancomycin is the most reliable and effective drug for treating MRSA. The appearance of MRSA with reduced susceptibility to vancomycin (vancomycin-intermediate *Staphylococcus aureus* [VISA]) is concerning and may be a warning that strains resistant to vancomycin could soon appear. SEARCH is a network of voluntary participants (i.e., hospitals, private industries, professional organizations, and state health departments) which have joined together to repo the isolation of *Staphylococcus aureus* with reduced susceptibility to vancomycin. All U.S. healthcare organizations or practitioners are encouraged to report such isolates to SEARCH and, after notifying their state health department, to send the isolates to CDC for confirmatory testing. SEARCH enhances the ability to detect these pathogens, which have a high public health importance but are difficult to detect through traditional surveillance systems, and provides confirmatory diagnostic and expedited susceptibility testing for these isolates when local testing is not feasible.	Ongoing. In 2001, laboratories participating in SEARCH processed over 300,000 *Staphylococcus aureus* isolates. Of these, 24 strains were sent to CDC for expedited vancomycin susceptibility testing. CDC confirmed 1 VISA and 7 strains with reduced susceptibility to vancomycin or near-VISAs (vancomycin MIC=4 µg/ml). To date, CDC has identified eight VISAs in the United States.
CDC	MRSA carriage in rural Alaska	In recent years, several community outbreaks of MRSA skin infections have occurred among Alaska Natives. This is a survey of the frequency of MRSA nasal colonization in 12 rural Alaska communities. The findings will be disseminated to affected communities and health care providers to help promote appropriate antimicrobial drug use and promote prevention of MRSA skin infections.	Ongoing.

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CDC	Antimicrobial resistant early-onset sepsis and maternal intrapartum antibiotic use	Increased use of antibiotic prophylaxis during labor and delivery to prevent perinatal group B streptococcal (GBS) disease has decreased the rate of early-onset GBS infections by 70%. As more antimicrobial drugs are used in the labor and delivery setting directed at prevent mother-to-child transmission of group B streptococcus, the risk that among newborns exposed to other perinatal pathogens, such as *E. coli*, drug resistant infections might actually increase. The objectives of this project were to determine the rate of early-onset infections with drug resistant *E. coli* in selected areas, to evaluate whether antimicrobial drug use during labor and delivery was associated with an increased risk of drug resistant *E. coli*, and to assess the impact of a penicillin G shortage on prophylactic use of penicillin, ampicillin, and other agents during labor and delivery.	Near completion. Despite the use of intrapartum antibiotics in nearly 1 in 3 deliveries, the project has thus far detected no increase in the rate of ampicillin resistance among *E. coli* that infect newborns in the first week of life.
CDC	Vancomycin-tolerant and vancomycin-resistant *Streptococcus pneumoniae*: developing a preparedness plan and enhancing surveillance	Recently, clinical isolates of *S. pneumoniae* that can survive, but not reproduce, in the presence of vancomycin (vancomycin-tolerant strains) were identified. Investigations of the biological mechanism of vancomycin tolerance suggest that tolerance may also be a precursor to vancomycin resistance. This project will evaluate the reproducibility of vancomycin-tolerance testing, determine the prevalence of vancomycin tolerance among pneumococcal meningitis patients in the U.S., and evaluate the clinical implications and identify risk factors for meningitis caused by vancomycin-tolerant pneumococci. In addition, CDC will develop a preparedness plan for the investigation and control of vancomycin-resistant pneumococci, should it emerge.	Ongoing. In FY 2001, confirmed reproducibility of vancomyci tolerance testing in an independent laboratory and began developing a simpler assay for use by multiple laboratories.

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CDC	The *Helicobacter pylori* Antibiotic Resistance Program (HARP): antimicrobial resistance in *Helicobacter pylori* in Alaska	HARP conducts prospective, long-term monitoring of trends in antimicrobial resistance to guide treatment regimens for *H. pylori infections*. 12 academic medical centers throughout the United States submit *H. pylori* isolates and clinical and epidemiologic data from endoscopically-diagnosed patients monthly. Resistance is tested at CDC. Resistance and epidemiologic data are entered into a database at CDC for analysis of prevalence, risk factors and regional trends in rates of antimicrobial resistance in H. pylori strains. The monitoring laboratory is also used for ongoing collaborative CDC-Emory-Veterans' Administration Medical Center research of *H. pylori* and peptic ulcer disease, and is a future platform for collaborative studies between academia, public agencies, and industry. A sentinel surveillance system for *H. pylori* has been established in Alaska to monitor antimicrobial resistance among Alaska Natives who have high rates of *H. pylori* infection; and where antibiotic resistance among *H. pylori* is higher in Alaska than reported elsewhere in the U.S	Ongoing. In FY 2001, susceptibility testing methods established by FDA and National Committee on Clinical Laboratory Studies (NCCLS) for antimicrobial testing of type strains of *H. pylori* were validated and the minimum inhibitory concentration with quality control limits for antimicrobial agents such as amoxicillin, clarithromycin, metronidazole, and tetracycline were determined. A line probe assay (LiPA) technique has been evaluated and standardized for use as a reference molecular subtyping method. Guidelines drafted for the diagnosis and treatment of *H. pylori* in Alaska Natives are under review.
CDC	Molecular tools for the control and epidemiology of head and body lice	Evaluate new molecular tools for monitoring louse population and determining the role of insecticide resistance in louse infestations and re-infestations to design and implement appropriate control strategies. Characterize local populations of lice and the global relationships and movements of louse populations. Ascertain the genetic relationships of head, body, and pubic lice. When completed, the data generated will improve knowledge of the epidemiology of insecticide resistance in louse populations and improve prevention and control strategies.	Ongoing. In FY 2001, collected head and body lice from over 10 states and 7 countries, and sequenced over 700 clones from gene libraries.

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CDC	Testing of drug-resistant *Trichomonas vaginalis*	Trichomoniasis is the most common curable STD in young, sexually active women. This project includes passive surveillance for *Trichomonas vaginalis* resistance among isolates from patients whose infections has not resolved after at least two courses of standard metronidazole therapy. Parasites are tested both aerobically and anaerobically for sensitivity to metronidazole and to tinidazole, which, outside the United States, is the most common alternative therapy for trichomoniasis. These data will identify molecular markers of metronidazole-resistant strains, allow investigation of drug-resistance mechanisms, and will be utilized to identify alternative chemotherapeutic agents.	Ongoing. Testing is an ongoing service of CDC. In FY 2001, initiated testing on isolates obtained through the Grady Adolescent STD Project (GRASP) to determine the prevalence of metronidazole-resistant *T. vaginalis* isolates in an urban adolescent clinic.
CDC	Enhanced surveillance of influenza viruses for resistance to licensed drugs and development of tests for rapid detection of drug-resistant strains with pandemic potential	Improved molecular tests for rapid diagnosis of mutants resistant to both the old and new drugs are needed for pandemic preparedness as well as for interpandemic control of influenza. This project studies avian influenza viruses of different subtypes, which will improve pandemic preparedness. In addition, it will evaluate existing biochemical tests and develop new molecular techniques for detecting influenza A and B mutants resistant to neuraminidase inhibitors (NIs), which will improve surveillance for drug-resistant variants among human influenza viruses.	Ongoing. In FY 2001, compared assays for resistance of influenza viruses to NIs to determine the most adequate method for further use in detecting of NI-resistant strains, and analyzed sequencing data available for avian influenza viruses with the goal of developing molecular techniques for rapid diagnosis of adamantane (amantadine or rimantadine)-resistant mutations among avian influenza viruses of different subtypes was initiated.
DoD	Development of a DoD AR surveillance plan consistent with the national AR surveillance plan	Establish an overarching framework for facilitating the implementation, operation, and evaluation of activities in AR surveillance within DoD.	Conducting discussions with leaders in infectious disease, laboratory, and preventive medicine in the three services to determine need and to develop practical approaches to plan development.

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DoD	DoD antimicrobial resistance surveillance network	Under a Cooperative Research and Development Agreement (CRADA) with private industry, developing a DoD-wide antimicrobial resistance surveillance network for identifying AR occurrences and trends within the military population. The cornerstones of this mechanism are: 1) the provision of daily, independent quality-assurance review and feedback of a military laboratory's susceptibility test results by experts in the field, 2) the continuous generation of up-to-date antibiograms based on an individual medical facility's AR patterns, 3) access to validated information on antimicrobial resistance occurrences and trends in the facility's geographic region for evaluating their implications for military personnel, and 4) facilitation of DoD-wide monitoring of AR trends to improve evidence-based decision and policy making on antibiotic usage and patient care, and 5) to enhance DoD ability to identify and respond to AR events of military significance in a timely manner.	Electronic antimicrobial susceptibility testing quality assurance and analysis system installed in 3 pilot sites completed. Expansion of project to additional sites under consideration for this year. An evaluation mechanism for determining utilization and effectiveness of system for the generation of antibiograms and recognition of trends at participating sites being developed. Linkage of sites into a DoD network for information sharing and analysis of AR trends to be initiated within the next year. Evaluation of network capability and effectiveness to be conducted in 2-3 years.
DVA	Emerging Pathogens Initiative (EPI)	The Veterans Health Administration (VHA) currently has an ongoing and well-defined AR surveillance plan (the EPI, a laboratory-based automated surveillance system).	Currently over 170 VHA facilities across the country transmit data to the EPI monthly. The data collected by the EPI are reviewed quarterly by the Infectious Diseases Program Office and reported to the Veterans Integrated Service Networks.
FDA	Proposed Rule – Surveillance/Reporting	Publish proposed rule regarding surveillance and annual reporting (included with proposed rule "Safety Reporting for Human Drug and Biologic Products").	Under Agency and Department review.
FDA	Guidance	Develop guidance relating to surveillance and annual reporting (based upon proposed rule "Safety Reporting for Human Drug and Biologic Products").	Awaiting final rule: surveillance and annual reporting.
CDC, FDA	Surveillance Planing	Coordinate surveillance activities.	Initial meeting held with CDC April 25, 2001; further discussion ongoing.

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Action Item #3: Develop Standards and Methodologies.			
CDC	A surveillance system for tracking and characterizing drug treatment failures in*Pneumocystis carinii* pneumonia	Because of the widespread use of trimethoprim-sulfamethoxazole and atovaquone for treatment and prophylaxis of PCP, AR monitoring is of great importance. Because direct sensitivity testing is currently not possible wit human *P. carinii*, work in this area has focused on molecular methods that look directly for mutations in the genes that encode the specific enzymes that are targeted by anti-*Pneumocystis* drugs. This project will study specific mutations at genetic positions that determine key drug enzyme-binding sites in an effort to correlate these mutations with treatment and prophylaxis failure data that are collected through patient questionnaires and chart abstractions. The results of this study will indicate where resistance appears to be in the process of emerging and whether continued or mor widespread surveillance is indicated.	Ongoing. Analysis completed for specimens and data collected to date and manuscript in press.
CMS	Rural Antibiotic Decision-support and Resistance Project (RADAR)	This CMS project is developing a Web-based system to provide expert antibiotic decision support and infection contr assistance to providers in small rural hospitals that lack infectious disease and infection control resources.	Evaluation in 2 pilot states (Idaho and Utah) will be complete 2002.
DVA	Emerging Pathogens Initiative (EPI)	The VHA uses standardized definitions and methods to set local parameters for surveillance in the EPI system. Current EPI data regarding some AR organisms are returned to the Veterans Integrated Service Networks quarterly with reporting station specific data included. National quartiles are also provided for use at the Network and local level. Confidentiality is a key element in any activity undertaken by the VHA. Great effort has been put forth to maintain confidentiality of the Emerging Pathogens Initiative surveillance data set. Access is strictly limited for any data with unique identifiers.	Automated surveillance.

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Action Item #4: Address Additional Surveillance Issues Unique to AR.			
CDC	Specialized surveillance projects and treatment trials for drug-resistant tuberculosis	Information on the initial drug regimen prescribed, coupled with information on initial drug susceptibility results, allows a judgment about the adequacy of therapy and corrective actio on individual cases of tuberculosis by public health officials and health care providers, if the regimen is judged to be inadequate or suboptimal. To improve knowledge of drug resistance in tuberculosis and effectiveness of alternate treatment regiments, CDC is conducting projects on the frequency of low-level INH resistance and resistant to quinolones, treatment of HIV-related tuberculosis using a rifabutin-based regimen, and a trial to determine the effectiveness of a new regimen for isoniazid-resistant tuberculosis. Results of these studies will describe prevalence and incidence of understudied resistance in tuberculosis and inform recommendations for new treatment regimens.	Ongoing.
CDC	See Action Item #5 (monitoring antimicrobial use in community and correlating usage with resistance patterns).	See Action Item #5 (Monitoring antimicrobial use in community and correlating usage with resistance patterns).	See Action Item #5 (Monitoring antimicrobial use in communit and correlating usage with resistance patterns).
FDA	Antimicrobial surveillance plan	Development of a surveillance plan for antimicrobial drugs with attributes of a surveillance system we would find useful—the quantity and quality of data we would need	Drafting a contract proposal is being to obtain a commercial database that contains antibiotic usage data as well as data on the emergence of resistant pathogens.
FDA	See Action Item #2 (Proposed Rule - Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule -Surveillance/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #5: Develop and Implement Procedures for Monitoring Antimicrobial Use In Human Medicine, Agriculture, Veterinary Medicine, and Consumer Products.**			
CDC	AUR: component of the National Nosocomial Infections Surveillance (NNIS)	The AUR component of NNIS allows participating hospitals t collect data on AUR and AR data resulting in a national estimate of the prevalence of antimicrobial-resistant organisms in hospitals and the amounts of antimicrobial agents used in these hospitals. These data allow select AUR rates to be compared among hospitals and provide better understanding of the relative importance of antimicrobial drug use vs. other factors (i.e., cross-transmission, severity of illness) for development of antimicrobial-resistant infections by several key pathogens (currently MRSA, with plans to include imipenem-resistant*Pseudomonas aeruginosa* and ceftazidime-resistant*Enterobacter* spp.)	Ongoing. In FY 2001, implemented the AUR component and received data from 15 hospitals.
CDC	Monitoring antimicrobial use in the community and correlating usage with resistance patterns	Analysis of antimicrobial use databases has proven to be complex, requiring sophisticated statistical methods to adjust for the design of certain usage survey samples and requiring substantial medical consultation time to link drug use with appropriate clinical diagnosis codes and potentially with databases regarding resistant infections. This project will develop a core analytic team that will track antimicrobial drug use in the community and correlate results of use with drug-resistance patterns (using drug-resistant*Streptococcus pneumoniae* as the marker community-acquired respiratory organism) and with community intervention efforts. The team will review availability and appropriateness of antimicrobial use databases and focus on establishing baseline trends in prescribing for upper respiratory infections using NAMCS, National Hospital Ambulatroy Medical Care Survey (NHAMCS), state Medicaid databases, Synergy, and other databases provided through partners (e.g., Blue Cross/Blue Shield; specific managed care organizations).	Ongoing. In FY 2001, analyzed and published trends in prescribing for respiratory conditions in the community during the 1990s by using NAMCS and NHAMCS, initiated development of standard programs and documentation for regular analyses of three national or regional databases for drug prescribing, and provided technical support to 5 intervention programs or partners. Antimicrobial use monitoring team examined antimicrobial usage in the context post-exposure prophylaxis for inhalational anthrax – analyzing 10 day and 30 day adherence and side effects in approximately 9,000 persons initiated on 60-days of post-exposure prophylaxis in Florida, D.C., New Jersey, and New York during the bioterrorism attack of 2001.

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CDC	National Ambulatory Medical Care Survey (NAMCS)	An annual national survey designed to meet the need for objective, reliable information about the provision and use of ambulatory medical care services in the United States. Findings are based on a sample of visits to nonfederally employed office-based physicians who are primarily engaged in direct patient care. NAMCS monitors trends in prescriptio of antimicrobial drugs in the outpatient setting.	Ongoing. Recent NAMCS methodology, data, and reports are available on the internet: (http://www.cdc.gov/nchs/about/major/ahcd/ahcd1.htm#Publications).
CDC	MRSA prevalence in patients with end-stage renal disease, health care workers, and their household contacts	Infection with MRSA is often preceded by colonization. Disease does not develop in most persons who are colonize but they can spread the organism to individuals at high-risk for infection, resulting in colonization and subsequent infection. Data are limited on the prevalence of colonization healthcare personnel in non-outbreak settings in the United States, and no data exist on prevalence among household contacts; furthermore, the consequences of MRSA colonization, particularly in healthy persons, are not well understood. This project measures the prevalence of, and risk factors for, MRSA colonization in target populations and follows outcomes prospectively for MRSA-colonized individuals and selected controls. If the prevalence of MRSA colonization in high-risk patient populations, healthcare personnel, and household contacts is measured, data can be used to design intervention strategies, including revised infection control measures, to be implemented by state and local health departments in healthcare settings and in the community to prevent the spread of MRSA colonization.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* in healthcare facilities	This project supports the development and implementation of comprehensive programs to reduce the incidence of MRSA infections in states and/or large regional networks acute phase and nonacute phase healthcare facilities. The Pittsburgh Regional Healthcare Initiative (PRHI) was recruited as a collaborating partner for this project. PRHI is a coalition of regional healthcare facilities and civic, corporate, and healthcare leaders in the Pittsburgh area dedicated to improving the quality of healthcare delivery in southwestern Pennsylvania. An intervention plan is being developed which involves applying a process engineering technique borrowed from the automotive industry Toyota Production System) TPS) to the processes of patient care that contribute to the problem of AR. The technique is designed to maximize the quality and efficiency of complex systems of work. Improving the design and flow of work should remove barriers to compliance with recommended prevention strategies.	Ongoing. Initiated pilot testing of the interventions has been in 2 hospitals within the network (University of Pittsburgh Medica Center-Presbyterian Hospital and Pittsburgh Veterans Administration Hospital). Thirty hospitals in the Pittsburgh metropolitan area (includes 69 intensive care units) are reporting infection data to CDC using standardized NNIS methodology, and facility-specific and aggregated region wide data are being fed back to PRHI quarterly. This system can be used to prospectively track the prevalence of MRSA among healthcare-associated infections.
DoD	Prescription databases	In 2001, DoD developed a prescription database as part of a patient safety program. This database is used principally to screen for drug-drug interactions resulting from patients fillin their prescriptions in more than one medical treatment venue Its linkage to a DoD syndromic surveillance system (ESSENCE) is being attempted. Once this is achieved, and when the AR surveillance system is more mature, a further link is planned to permit trends in detected AR to be analyzed with respect to prescription practices and patient presentations.	Initiated prescription database. Linkages are being developed or considered for development.
DVA	Emerging Pathogens Initiative (EPI)	Resistance data are being gathered in the EPI, an automated surveillance system, at the reporting site level and can be used for comparisons based on geographic areas and can be linked to ICD-9-CM diagnostic codes. In addition, drug use data can be linked to laboratory testing and diagnoses, particularly as it relates to hepatitis C, a significant emerging disease.	This item is already underway in the VHA with reporting from facilities across the country.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	N/A	Review private sector surveillance data to determine whether it has potential to support FDA/CDER regulatory and scientific activity.	Currently (March 2002) drafting a contract proposal to obtain commercial data to explore its potential usefulness.
FDA	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Surveillance/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).
Action Item #6: Identify and Evaluate Methods for Collecting (e.g., Optimal Sampling Methods) and Disseminating the Surveillance Data on Antimicrobial Drug Use.			
FDA	N/A	Review private sector surveillance programs (availability 6-12 months).	A contract proposal is being drafted to obtain a commercial database that contains antibiotic usage data as well as data on the emergence of resistant pathogens.
FDA	See Action Item #2 (Proposed Rule Surveillance/Reporting).	See Action Item #2 (Proposed Rule Reporting/Reporting).	See Action Item #2 (Proposed Rule Reporting/Reporting).
FDA	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).	See Action Item #2 (Guidance).
Action Item #7: Work With Accrediting Agencies To Address Antimicrobial Drug-Use As Part Of Quality Assurance In Health Care Delivery Systems.			
CMS	National Surgical Infection Prevention Project (SIPP)	This CMS project promotes utilization of appropriate antibiotics for surgical prophylaxis and discontinuation within 24 hours after surgery. It involves collaboration with JCAHO and 16 other organizations. See www.surgicalinfectionprevention.org for details.	Development complete. Medicare quality improvement organizations (QIOs) begin fieldwork in August 2002.
Action Item #8: Ensure That Clinical Laboratories That Provide Data for AR Surveillance Purposes Have Access to and Routinely Participate in Pertinent Training and Proficiency Testing Programs with Good Performance and Indicate AR Testing Methodologies in Their Surveillance Reports (e.g., Specific Automated Methods or Manual Techniques).			
CDC	Lab Errors: CD-ROM for susceptibility testing	This CD-ROM will provide all of the materials necessary to train laboratory workers to test bacterial isolates for resistance to antimicrobial agents and issue accurate reports to physicians to help them choose the best antimicrobial agents to treat infections. A better understanding of the importance of using standardized methods has been realized. Ultimately the accuracy of antimicrobial susceptibility testing and reporting should be achieved. This CD-ROM has the potential to become a standard teaching tool in medical technology programs and for training infectious disease fellows about antimicrobial resistance.	Near completion. Portions of the CD-ROM program have been used already in national conferences to teach microbiologists and infectious disease specialists about the proper methods of testing and interpreting antimicrobial susceptibility tests. The CD-ROM is undergoing beta-testing now to ensure that the programs are working correctly. The CD-ROM course will be used in a statewide initiative in Washington to improve antimicrobial susceptibility testing and reporting.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Multilevel Antimicrobial Susceptibility Testing Educational Resource (M.A.S.T.E.R.) Program	The M.A.S.T.E.R. program, is a 3-phase project to upgrade the accuracy of antimicrobial susceptibility testing and reporting in the U.S. Currently, the Web site has case studies, a Q and A section, hot papers, and a list of references. A CD-ROM training course in susceptibility testing is nearly completed. A "Train of Trainers" session for antimicrobial susceptibility testing methods was undertaken i collaboration with the Washington State Health Department and offered to laboratorians from 5 states. Both the MASTER Web site and CD-ROM materials were used for training. The course was completed April 18, 2001.	Project ongoing. Expanation to more states expected in 2002.
CDC	Reducing laboratory errors associated with detecting and reporting antimicrobial-resistant bacteria from blood cultures (Iowa)	The goal of the Iowa project is to assess the accuracy of the bacterial identification and antimicrobial susceptibility testing data appearing in patients' charts in 15 hospitals for organisms isolated from positive blood cultures. Blood culture isolates are sent to CDC for confirmation of identification and susceptibility testing. These results are compared to the results from the original laboratory report and the results retrieved from the patients' charts. The accuracy of the reports and the appropriateness of the antimicrobial agent reported are assessed. This project should provide important feedback information regarding inappropriate reporting of test results to the patients' charts and thus improve laboratory accuracy. By reporting only necessary AR results to the patients' charts, we should, in turn, improve antimicrobial prescribing in the hospitals in the study.	Ongoing. To date, blood culture isolates have been collected from 16 different hospitals in Iowa, identifications and susceptibility test results have been completed at CDC, and the results are being collated and reviewed with other data in Iowa.
CDC	Antimicrobial resistance research and reference testing	CDC reference laboratory conducts ongoing research and provides selected reference services for susceptibility testing of numerous bacterial species.	Ongoing. Recent achievements include the description of ne AR mechanisms, which has led to modification and improvement of the testing methods used in clinical microbiology laboratories to detect resistance, evaluations of NCCLS methods completed and modifications made to improve accuracy, and evaluations of commercial susceptibili testing methods completed and problems noted to the manufacturers.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	*Mycobacterium tuberculosis* (Mtb) antimicrobial susceptibility testing program	Approximately 160 laboratories participate in this program designed to assess and enhance the ability of clinical laboratories to accurately test for AR. Most laboratories test for susceptibility to isoniazid, pyrazinamide, ethambutol and rifampicin, and streptomycin. Approximately 35 laboratories test nontuberculous mycobacteria in addition to susceptibility to other drugs. Laboratories can view reports of results on a Web site address for each panel shipment for feedback.	Ongoing.
Action Item #9: Evaluate the Performance of Licensed, Automated AR Testing Devices in the Context of Changing Resistance Patterns and Update Their Labeling When Appropriate (e.g., Changes in Quantitative Resistance That May Make a Test Result Invalid).			
Action Item #10: Working with Partners, Including National Committee for Clinical Laboratory Standards (NCCLS), Further Develop, Refine, and Promote Standardized Clinical, Epidemiologic, and Laboratory Methods for Documenting and Assessing the Significance of Drug Resistance Among Yeasts and Moulds, Parasites, and Viruses.			
FDA	Devices containing antimicrobials	Advanced notice of proposed rulemaking: how to regulate devices which contain antimicrobial agents in light of public health concerns regarding AR.	Moratorium on rulemaking—awaiting clearance
FDA	In-vitro antimicrobial susceptibility testing	Develop quality control standards for the in-vitro antimicrobial susceptibility testing of bacterial pathogens isolated from aquaculture foods.	Initiated studies FY 2001.
FDA	Devices containing antimicrobials guidance	Draft guidance document for industry: how the Center for Devices and Radiologic Health (CDRH) intends to regulate devices containing antimicrobial agents, and what information regarding efficacy and resistance CDRH wants to see in premarket applications (interim until rulemaking is completed).	Draft circulated inside Office of Device Evaluation, February 2002.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #11: Identify Ways To Overcome Economic, Legal, and Other Barriers To Appropriate AR Testing and to the Reporting of Results (e.g. Sufficient Human Resources, Cost Considerations, Empiric Treatment Recommendations, Managed-Care Practices, etc.).			
CDC	Economic modeling of diagnostic and treatment strategies for gonorrhea based on prevalence of antimicrobial resistance	The increasingly widespread use of nonculture methods for gonorrhea diagnosis is a major challenge to monitoring AR in *N. gonorrhoeae*, especially in light of the emergence of ciprofloxacin-resistant gonococcal isolates from Hawaii (ciprofloxacin is first-line gonorrhea therapy). This project will examine which diagnostic and treatment strategies are more cost-effective when the proportion of *N.gonorrhoeae* that are ciprofloxacin-resistant is less than 5%: continue to use ciprofloxacin and implement more widespread susceptibility testing, or switch to a more expensive cephalosporin and not increase the scope of susceptibility testing. When completed, the results will help provide a rational basis for programmatic decisions both for selection of gonorrhea treatment and for use of laboratory resources.	Analysis ongoing. Manuscript in progress.
Action Item #12: Pursue Legal Mechanisms for Manufacturers To Provide Otherwise Unavailable Drugs to Government Reference Laboratories for the Sole Purpose Of Antimicrobial Drug Susceptibility Testing (as part of surveillance) with the Understanding That These Drugs Will Not Be Used for Drug Discovery Purposes.			
Action Item #13: With State Health and Agriculture Departments and Other Stakeholders, Define Needed Core Capacity (Human, Laboratory, and Electronic Resources) at the State and Local Level To Ensure That Basic AR Surveillance Is Conducted In These Jurisdictions. As Part of This Effort, Ensure That State Public Health and Veterinary Diagnostic Laboratories Maintain the Capacity To Test the Drug-Susceptibility Patterns of Resistant Organisms of Public Health Importance, Especially For Drug-Microorganism Combinations for Which Testing Mechanisms Are Not Routinely Available at Hospital and Commercial Laboratories.			
Action Item #14: Provide Resources To Assist In Meeting State and Local Core Capacity Needs for AR Surveillance. Strive To Provide Consistent Funding from Year to Year to State and Local Health and Veterinary Diagnostic Laboratories That Meet Quality Assurance Standards.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #15: Provide an Accessible, Centralized Source of AR Data from Major Surveillance Systems Involving Animal and Human Populations. In Consultation with Stakeholders, Determine How To Report AR Data in a Way That Is Valid and Useful to Interested Parties (e.g., Clinicians, Public Health Officials, Veterinarians, and Researchers). Include Sufficient Detail in Surveillance Reports To Permit Local Analysis and Comparison with Trends in Drug Use and Medical and Agricultural Practices.			
CMS	Prevention of AR in the outpatient setting	This CMS demonstration project in Colorado evaluates a combination of patient and provider education to minimize the inappropriate use of antibiotics in the outpatient setting. It also evaluates the use of Medicaid and managed care prescription data as indicators of providers' antibiotic-prescribing patterns for Medicare patients (Medicare does no have a prescription drug benefit in its fee-for-service component).	Project will be completed in 2002. Results could be applied in all 50 states.
DoD	Surveillance for *Streptococcus pyogenes* among military trainees	Increasing resistance to macrolide antibiotics has been demonstrated for *S. pyogenes* isolates. Furthermore, during military-recruit training exercises, penicillin-allergic patients are often given erythromycin when mass prophylaxis is recommended. If resistant organisms are present or develo in this population, *S. pyogenes* infections (latent or overt) may not be treated effectively. Recruits could become reservoirs of resistant pathogens for military populations. This project conducts antimicrobial susceptibility and emm-gene typing on *S. pyogenes* isolates collected from recruits at military training centers and monitors for *S. pyogenes* resistance rates. As of September 2001, the resistance rates detected in the recruit population were the following: erythromycin (8%), clindamycin (3%), and tetracycline (7%). Resistance differed by emm-gene type, with types 6, 3, 29, 2, 12, 1, and 75 accounting for more than 75% of the typed isolates.	Reports of susceptibility test results and summary statements are being provided to the primary care facility, are accessible to DoD staff on the Web site www.geis.ha.osd.mil and have been used in presentations at national meetings. Generated data show moderate AR rates as of 2001.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Surveillance of antibiotic-resistant *S. pneumoniae* in military populations	Antibiotic resistance in *S. pneumoniae* has risen dramatically over the last decade, with varying levels of resistance found different regions of the country. Similarly, *S. pneumoniae* causes significant morbidity among populations served by U.S. military medical centers. In this study, *S. pneumoniae* isolates from selected U.S. military medical centers are being serotyped, subtyped, and tested for antibiotic resistance. As of September 2001, full or partial penicillin resistance was found in 34% of the isolates, with 22% having resistance to or more antibiotics. Serotypes 6, 9, and 19 have been found to be associated with increased penicillin resistance.	Reports of resistance findings and trends are being shared with the contributing medical centers, and summary statements are available through the Web site http://www.geis.ha.osd.mil Study findings have been presented at national meetings and in peer-reviewed publications.
Action Item #16: Provide Healthcare System Administrators and Other Decision Makers with Data on the Impact of Drug-Resistant Organisms (e.g., Outcome, Treatment Costs) and on Effective Prevention and Control Measures.			
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research	The University of Pennsylvania Center for Education and Research on Therapeutics has undertaken studies on AR with the Veterans Affairs Medical Center in collaboration with Health Services Research and Development Service, Department of Veterans Affairs, and with hospitals in the Delaware Valley in collaboration with NIAID.	The University of Pennsylvania Center for Education and Research on Therapeutics has undertaken studies on AR with the Veterans Affairs Medical Center in collaboration with Health Services Research and Development Service, Department of Veterans Affairs, and with hospitals in the Delaware Valley in collaboration with NIAID.
Action Item #17: Expand and Enhance Coordination of Surveillance for Drug-Resistance in Enteric Bacteria In Sick and Healthy Humans and in Sick and Healthy Animals on Farms, at Slaughter, and at Retail.			
FDA	AR DNA in feed ingredients	Assess the prevalence of antibiotic-resistant DNA in feed ingredients , primarily rendered product. This work will be done in conjunction with FDA field personnel when they inspect renderers for compliance with the bovine spongiform encephalopathy (BSE) regulation. Results will be incorporated into NARMS.	Ongoing.
Action Item #18: Evaluate the Usefulness of Monitoring Sentinel Human Populations (e.g., Farm, Abattoir, Fruit and Vegetable, and Food Processing Plant Workers) and Persons in the General Community for Infection or Colonization with Resistant Enteric Bacteria.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #19: Conduct Pilot Studies To Assess the Extent of Environmental Contamination by Antimicrobial Drug Residues and Drug-Resistant Organisms That Enter the Soil or Water From Human and Animal Waste. If Contamination is Detected, Conduct Appropriate Surveillance in Waste, Surface and Ground Water, and Soil from Agricultural Areas in Which Waste Is Used for Fertilizer, and Conduct Studies To Determine Potential Impact on Human and Animal Health.			
Action Item #20: Gather Information on the Relationship Between Antimicrobial Pesticide and Herbicide Use and the Emergence of Drug-Resistance by Monitoring.			
Focus Area II: Prevention and Control			
Action Item #21: Identify Factors That Promote or Impede Appropriate Drug Use in Hospitals, Extended Care Facilities, and Outpatient Settings In Collaboration with Partners.			
AHRQ	Research Program Project (P01): understanding and eliminating health disparities in blacks, project 2	Economic Access to Antiretroviral (ARV) prescription drugs and adherence to ARV Guidelines for African American Medicaid Enrollees with AIDS or HIV Disease in South Carolina.	Medical University of South Carolina program under way to increase the number of providers treating to current guidelines.
AHRQ	Research Projects (R01): online commentary use and antimicrobial prescribing. Trial to reduce antimicrobial prophylaxis errors	Online commentary is talk that describes what a physician is seeing, feeling, or hearing during the physical examination of a patient; the researchers examined the relationship between online commentary use and physicians' prescribing decisions. The trial will assess methods to avoid mistimed administration of preoperative antimicrobial agents.	Physicians who used “no problem” online commentary (e.g., “her ears look perfect”) prescribed antibiotics less often than physicians who used “problematic” online commentary.
AHRQ	Research demonstration and dissemination project (R18): HIV treatment error reduction using a genotype database	This project aims to design and implement an automated system that will integrate HIV genotypic testing results with corresponding patient medication data within an electronic medical record system to reduce antiretroviral prescribing errors and improving antiretroviral drug selection. A second aim is to assess the efficacy and usability of this system in a community-based, Ryan White-funded outpatient setting serving a predominantly urban, minority, and low-income population.	Data to be measured and analyzed are the frequency of rules triggered, provider responses to alerts, and clinical outcomes measured by HIV viral load. Clinical outcomes will be statistically analyzed as success or failure by absolute viral load and its relative reduction. Both analyses will look at correlation of success or failure with the presence or absence of an alert and the provider response to alerts. System usability by providers will also be assessed qualitatively.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research	The Harvard Pilgrim Healthcare CERT supports nine collaborating systems within an HMO Research Network to study antibiotic use in children.	A retrospective cohort study using automated record linkage is under way to determine rates of antibiotic use in pediatric patients and indications for therapy over time and across nine geographic regions.
CDC	See Action Item #63 (Wisconsin Antibiotic Resistance Network).	See Action Item #63 (Wisconsin Antibiotic Resistance Network).	See Action Item #63 (Wisconsin Antibiotic Resistance Network).
CDC	See Action Item #63 (The Chicago Antimicrobial Resistance Network).	See Action Item #63 (The Chicago Antimicrobial Resistance Network).	See Action Item #63 (The Chicago Antimicrobial Resistance Network).
CDC	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).
DVA	Appropriate use of antimicrobials	This is a rather broad-based Action Item that is currently addressed in the VHA facilities every day. The VHA has a national formulary, develops and implements care guidelines, and provides extraordinary educational opportunities for staff to deal with questions concerning appropriate use of antibiotics. This is an ongoing activity, but the effort will continue to be enhanced by further collaboration with federa agencies and other partners (including the private sector) since appropriate antibiotic usage involves many components such as physician education, education of the public, appropriate drug advertising, control of over-the-counter antibiotic use, and many other items that require intervention both inside and outside of the federal systems.	Ongoing.
FDA	Labeling Rule	The new labeling is intended to educate physicians and the public about the resistance problem and to encourage physicians to prescribe systemic antibacterial drugs only when clinically necessary.	Responded to comments on proposed rule; completed draft final rule; conducting CDER review.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #22: Develop Appropriate Drug Use Policies and Evaluate the Impact (Including on Prescribing Patterns, Resistance Rates, Patient Outcomes, and Cost) of Implementing These Policies in Hospitals and Other Health Care Delivery Settings. Identify Ways To Increase Adherence to Appropriate Use Policies Proven To Be Beneficial in Collaboration with Partners.			
AHRQ	Research Projects (R01): reducing antimicrobial resistance: a randomized trial. Otitis Media: parent education to avoid antibiotic use. Pediatric EBM—getting evidence used at the point of care. Minimizing antibiotic resistance in Colorado (MARC). Long-term outcomes of HIV care in the HAART era	Developing and testing physician- and patient-level interventions in entire communities in a randomized trial to determine if the interventions reduce prescribing and the prevalence of resistance. Randomized clinical trial to evaluate the need for antibiotic therapy during an episode of mild acute otitis media. Evaluation of whether use of an evidence-based decision-support system at the point of care will reduce frequency and duration of antibiotic therapy for otitis media and reduce duration of therapy for acute sinusitis Evaluation of the independent and combined marginal impact on antibiotic prescribing behavior and antibiotic resistance of two strategies for community education: 1) household- and office-based informational materials (small-scale community-based education) and 2) mass media (television, radio, print news, and Web site). One hypothesis to be examined is whether antiretroviral resistance leads to clinical failure more often with inexperienced providers.	All studies are currently in progress and should provide clinically applicable evidence that will decrease the unnecessary use of antibiotics.
AHRQ	Small research grant (R03): seeking and denying antibiotic treatment in pediatrics	Dissertation grant to examine issues developed by Heritage Stivers T. Online commentary in acute-phase medical visits: a method of shaping patient expectations.Soc. Sci. Med. 1999;49:1501-17. This paper conceptualizes a type of physician communication, termed “online commentary.” Online commentary is talk that describes what the physician is seeing, feeling, or hearing during physical examination of the patient. Some dimensions of online commentary are described, and its functions in routine and acute medical consultations are distinguished.	Using a case study method, the paper focuses on the role of online commentary in preempting patient resistance to upcoming “no problem” diagnostic evaluations which could delegitimize patients' decisions to seek medical assistance or deprive them of anticipated medical benefits. It is hypothesized that this role for online commentary may be associated with successful physician resistance to implicit or explicit patient demands for inappropriate antibiotic medication.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
AHRQ	Research Demonstration (U18): Centers for Education and Research on Therapeutics (CERTs) program: a national initiative to increase awareness of the benefits and risks of new, existing, or combined uses of therapeutics through education and research	The University of Pennsylvania CERT has begun studies on improving the use of antibiotics locally and nationally, on reducing the use of antibiotics for acute bronchitis in outpatients, on the effect of formulary changes on the resistance patterns of *Escherichia coli* and *Klebsiella spp.,* on antibiotic-resistance patterns from outpatients with acne who are receiving tetracycline and a group of patients who a not, on antibiotic use and infection with drug-resistant *Streptococcus pneumoniae* in the United Kingdom, on risk factors for infection due to fluoroquinolone-resistant *E. coli* and *K. pneumoniae,* on risk factors for fluoroquinolone resistance in infections due to extended-spectrum beta-lactamase-producing *E. coli* and *K. pneumoniae* and on adherence to protease inhibitors and adherence to nonnucleoside reverse transcriptase inhibitors in HIV infection.	Independent risk factors for fluoroquinolone resistance were fluoroquinolone use, aminoglycoside use, and long-term care facility residence. Clin. Infect. Dis. 2001;33:1288-94. Adherence to newly initiated antiretroviral therapy begins to wane after the first month; therefore, closer assessment of adherence, particularly after this first month, is important . AIDS 2001;15:2109-17.
AHRQ	Research demonstration (U18): optimizing antibiotic use in long-term care	Evaluation to determine if a clinical algorithm for managing urinary tract infections in older adults in residential long-term care facilities can reduce the overall use of antibiotics in long-term care facilities.	Nursing homes in Ontario and Idaho have been recruited, algorithms have been introduced, and data are being collecte Projected impact is that the rate of antibiotic prescribing at intervention sites will decrease.
CDC	Evaluation of routine cycling of antimicrobial agents	Routine cycling in the choice of empiric antimicrobial agents has been proposed as a means of limiting development of A mutants in hospitalized patients. This study in medical intensive care units at 3 institutions evaluates changes in prevalence of resistant target pathogens and patient outcomes during cycling interventions compared to baseline. The results will indicate whether cycling interventions have a protective effect on infection or colonization with resistant target pathogens and the impact of specific cycling periods on adequate therapy for suspected infections, length of hospital stay, and mortality rates.	Funds awarded in 2001. Data collection in progress.
CDC	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).	See Action Item #26 (Campaign to Prevent Antimicrobial Resistance in Healthcare Settings).
CDC	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (Partnerships with healthcare delivery organizations and insurers to promote appropriate use of antibiotics for outpatient upper respiratory infections).
CDC	See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Program (CARP).
DVA	See Action Item #21.	See Action Item #21.	See Action Item #21.
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #23: Evaluate the Relationship Between Prescribing Behavior and Specific Antimicrobial Drug Marketing and Promotional Practices. Assess the Public Health Effects of These Practices in Collaboration with Partners.			
FDA	N/A	Review "Direct to Consumer" (DTC) promotion as applies to antimicrobials.	Ongoing.
FDA	Industry guidance	Develop guidance for industry regarding resistance information to include in .	Awaiting publication of "appropriate use labeling" final rule.
Action Item #24: Help Individual Hospitals and Healthcare Systems Analyze How the Availability of AR Data and Computer-Assisted Decision Support Systems Influences Prescriber Behavior, Health Outcomes, and Costs. This Plan May Include the Provision of Computer Software and the Establishment of Projects That Involve the Medicare Peer Review Organizations (PROs).			
CDC	See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project (CARP).
CDC	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).	See Action Item #63 (IMPART - Inter-Mountain Project on Antimicrobial Resistance and Therapy).
CMS	Rural Antibiotic Decision-support and Resistance Project (RADAR)	This CMS project is developing a Web-based system to provide expert antibiotic decision support and infection contr assistance to providers in small rural hospitals that lack infectious disease and infection control resources.	Evaluation in two pilot states (Idaho and Utah) will be comple in 2002.
DVA	Emerging Pathogens Initiative (EPI)	Data on antimicrobial resistance with quartile rankings in the VHA nationwide are provided to the Networks, including reporting site-specific data by using the EPI, an automated surveillance system. This will be an ongoing initiative since it is not entirely clear what the best method for antimicrobial resistance feedback will be in the final analysis.	Ongoing at VA sites across the country.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #25: Conduct a Public Health Education Campaign To Promote Appropriate Antimicrobial Use as a National Health Priority. The Health Campaign Should Involve Many Partners.**			
CDC	National advertising campaign promoting the appropriate use of antibiotics	This national media education campaign is being developed to promote appropriate antimicrobial drug use in the community for upper respiratory infections, e.g., to decrease patient requests for antibiotics for illnesses for which they offer no benefit. Target audiences are parents of young children and healthy adults. The campaign will use a variety of health communication materials based on concepts tested in focus groups, and its effectiveness will subsequently be evaluated.	Ogilvy Public Relations Worldwide was awarded the contract in September 2001. National launch and media event are planned for the Winter 2002.
CDC	See Action Item #26 (State-Based Multifaceted Interventions and Council for Affordable Quality Healthcare).	See Action Item #26.	See Action item #26.
CMS	Prevention of antimicrobial resistance in the outpatient setting	This CMS demonstration project in Colorado evaluates a combination of patient and provider education to minimize the inappropriate use of antibiotics in the outpatient setting. It also evaluates the use of Medicaid and managed care prescription data as indicators of providers' antibiotic prescribing patterns for Medicare patients (Medicare does not have a prescription drug benefit in its fee-for-service component).	Project will be completed in 2002. Results could be applied in all 50 states.
FDA	Education/outreach plan	Education/Outreach plan regarding appropriate use of antimicrobials for consumers, health professionals, and health educators (includes Web site) (timeline 6-12 months)	Draft plan completed; discussions with CDC are ongoing; several concept proposals have been drafted and are currently under discussion in CDER.
FDA	See Action Item #23 (Industry Guidance).	See Action Item #23 (Industry Guidance).	See Action Item #23 (Industry Guidance).
FDA	See Action Item #23 (N/A).	See Action Item #23 (N/A).	See Action Item #23 (N/A).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #26: In Collaboration with Many Partners, Develop and Facilitate the Implementation of Educational and Behavioral Interventions That Will Assist Clinicians in Appropriate Antimicrobial Prescribing.**			
CDC	Campaign to prevent antimicrobial resistance in healthcare settings	This campaign focuses on preventing AR in healthcare settings, such as hospitals and long-term care facilities. An evidence-based 12-step program promotes 4 strategies for clinicians: 1) preventing infection, 2) diagnosing and treating infection effectively, 3) using antimicrobials wisely, and 4) preventing transmission. Variations of the 12 steps will be tailored to specific patient populations (e.g., dialysis, surgery, geriatrics, critical care, obstetrics, emergency care, pediatrics, and patients in long term care facilities). When these strategies are fully implemented and evaluated, improvements are anticipated in infection control, appropriate antimicrobial drug use and incidence of drug-resistant infections occurring in healthcare settings.	Established partnerships with Infectious Diseases Society of America (IDSA) and American Society of Microbiology (ASM) to gain their assistance in dissemination of campaign messages; developed initial educational materials for clinicians; created Web site; held initial rollout of campaign in March 2002.
CDC	State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections	The campaign assists states in implementing broad-based health communication and behavioral interventions to promo appropriate antibiotic use for outpatient upper respiratory infections. State health departments develop broad-based coalitions (e.g., state medical societies, healthcare delivery organizations, healthcare purchasers, consumer groups), us CDC educational materials, develop materials of their own, and launch campaigns targeting providers and the general public. Controlled trials have demonstrated success of this program in decreasing inappropriate prescribing; also, nationwide antibiotic prescribing rates for children are declining.	Funded 18 states in FY 2001.
CDC	Partnerships with healthcare delivery organizations and insurers to promote the appropriate use of antibiotics for outpatient upper respiratory infections	Work with Coalition for Affordable Quality Healthcare to implement educational and behavioral interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections in managed care organizations.	Implemented projects in 26 organizations, with 131 million members in FY 2001.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	Development of principles of appropriate antibiotic use for treatment of acute respiratory infections	Evidence-based principles of judicious use of antimicrobial agents for pediatric upper respiratory infections have been developed by representatives of CDC, the American Academy of Pediatrics, and the American Academy of Family Physicians (Pediatrics. 1998; 101:S163-S184). This follow-up project developed similar principles for adults. Most antibiotic prescriptions for adults in ambulatory practice are for acute sinusitis, acute pharyngitis, acute bronchitis, and nonspecific upper respiratory infections. To develop evidence-based prescribing principles for these conditions, CDC convened a panel of physicians representing the disciplines of internal medicine, family medicine, emergency medicine, and infectious diseases.	With the endorsement by the American College of Physicians, American Academy of Family Physicians, Infectious Diseases Society of America, and CDC, the principles were published in 2001 in the Annals of Internal Medicine (2001;134:479-529) and distributed to primary care physicians.
CDC	A medical curriculum promoting appropriate use of antibiotics	Topics include extent of antibiotic resistance, diagnostic techniques, and appropriate antibiotic use. Case studies focus on examination, diagnosis, treatment, and communication. This course is designed to meet the needs of a variety of medical schools with components that can be used separately or as a whole.	Produced multi-faceted educational design for the curriculum. Recruiting medical schools to participate in its evaluation, in collaboration with the Association of American Medical Colleges.
CDC	Reporting antimicrobial susceptibility data to clinicians	Assist NCCLS to produce guidelines for clinical microbiology labs on how to compile and report summaries of cumulative antimicrobial susceptibility data in a standardized manner to aid in clinical decisions. When completed and evaluated, standard reports should improve empiric prescribing, based on data of antimicrobial susceptibility testing and allow comparisons of data among hospitals.	Developed guidelines in FY 2001.
CDC	Activities of the National Center HIV, STD, and TB Prevention (NCHSTP)	NCHSTP has as its mission the prevention and control of HIV infections, sexually transmitted diseases, and tuberculosis.	Ongoing projects in collaboration with partners develop, assess, and update prophylaxis and treatment recommendations for these infections and facilitate their implementation.
CMS	Prevention of antimicrobial resistance in skilled nursing facilities	This demonstration project in Idaho evaluates the use of provider education and protocols to improve the diagnosis and treatment of urinary tract infection in nursing facility residents.	Project will be completed in 2002. Results could be applied in all 50 states. Because antibiotics are so heavily used in nursing facilities and much of the use is inappropriate, even a modestly successful intervention could have a substantial impact on antibiotic use.
CMS	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Development of an intervention to enhance the communication skills of primary care providers on the prudent use of antimicrobials	A workshop for enhancing healthcare provider communication skills in advising patients on the prudent use of antimicrobial agents. Workshop materials include 1) a video illustrating doctor-patient discussions on inappropriate antimicrobial usages; 2) a booklet containing recommendations on applicable communication techniques; and 3) a workshop agenda, syllabus, and other supporting materials. The result of the workshop is a heightened ability to manage discussions with patients on prudent antimicrobial use. Workshop effectiveness will be evaluated by an analys of workshop participant questionnaires completed at the end of the workshop; a follow-up survey on participant perceptior about improvements in communication skills, success in influencing patient demand for antimicrobial agents, and use of patient education materials on the prudent use of antimicrobial agents; and a review of pre- and post-workshop antimicrobial prescribing rates by participating primary care providers; and assessment of training effectiveness.	Completed research to identify existing and relevant educational programs and materials, to determine which continuing medical education style and intervention strategies are most appropriate for the DoD health care setting, and to identify areas of primary care provider communication skill development requiring improvement. A variety of communication approaches currently used by primary care providers are being assessed for relevance to the topic of prudent usage of antimicrobial agents. It is anticipated that workshops can be conducted later this year.
DVA	Prudent use of antibiotics interventions	The VHA is already involved in many of these activities with particular emphasis on educational activities and training for prescribers at all levels, including physicians, nurse practitioners, and others who are involved with the direct care of patients. Particularly, the VHA provides a strong role in education for health professions students, medical and nursing trainees, and others critical to the provision of care to patients such as social workers, psychologists, and advance role nurses. In addition, the VHA has produced guidelines, including those that relate to antimicrobial drug use. Therefore, the VHA is well underway for this action item.	Ongoing.
FDA	See Action Item #23 (N/A).	See Action Item #23 (N/A).	See Action Item #23 (N/A).
FDA	See Action Item #23 (Industry Guidance).	See Action Item #23 (Industry Guidance).	See Action Item #23 (Industry Guidance).
FDA	See Action Item #25 (Education/Outreach Plan) .	See Action Item #25 (Education/Outreach Plan) .	See Action Item #25 (Education/Outreach Plan) .

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #27: Explore Ways To Integrate Appropriate Use Information into Antimicrobial Package Inserts and Promotional Materials, To Provide Such Information to Patients with Each Prescription, and To Provide Clear Guidance to Industry To Ensure That Promotion of Antimicrobials Directed Towards Consumers Encourages Appropriate Use and Discourages Inappropriate Use.			
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #28: Articulate Factors That Support the Current Approach of Requiring Prescription-Only Dispensing for All Systemic (e.g., Nontopical) Antimicrobial Drugs Used In Clinical Medicine.			
Action Item #29: Periodically Review and Update Antimicrobial Drug Susceptibility Information Including In Drug Labeling, with Input from Stakeholders and Other Experts, e.g., the National Committee for Clinical Laboratory Standards (NCCLS) and CDC.			
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
Action Item #30: Convene an Advisory Panel or Other Expert Group in Involving Stakeholders and Partners To Consider Issues Related to Resistant Pathogens That Cause Serious Infections for Which Available Treatments Options Are Very Limited or Nonexistent.			
FDA	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).	See Action Item #21 (Labeling Rule).
FDA	See Action Item #23 (Industry Guidance).	See Action Item #23 (Industry Guidance).	See Action Item #23 (Industry Guidance).
Action Item #31: Convene A Working Group To Examine the Impact of Federal Reimbursement Policies for Home Parental Antimicrobial Treatment, Appropriate Antimicrobial Use, and Appropriate Use of Antimicrobial Susceptibility Testing. Where Needed, the Working Group Will Make Recommendations for Modifying These Policies.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #32: Develop and Submit Measures for Appropriate Antimicrobial Use to the National Committee for Quality Assurance for Inclusion in Health Plan Employer Data and Information Set (HEDIS), Which Provides Comparative Data on Managed Care Organizations			
CDC	Development and testing of HEDIS measures for appropriate antibiotic use	In this project, CDC epidemiologists collaborate with experts in the development and testing of HEDIS measures to develop and test one or more measures of appropriate antimicrobial use in children. Potential measures include rate of prescribing antimicrobial drugs for acute upper respiratory infections and bronchitis; rate of prescribing antimicrobial drugs for pharyngitis where no throat culture or rapid streptococcal antigen test was performed; and episodes of otitis media treated with a recommended first-line agent. If the measure is incorporated into HEDIS, the measure and its impact on physician and patient awareness of appropriate antimicrobial use will be evaluated.	Ongoing. Awarded contract in 2001 to Association of American Medical Colleges. In FY 2002, convened a multidisciplinary team to determine specifications for potentia measures, which will be tested in at least 5 health plans.
Action Item #33: Evaluate The Potential Impact Of Improved Diagnostic Tests, Including Rapid Point-of-Care Tests on Antimicrobial Drug Use and Patient Care, and Assess Their Financial Implications. Take into Account Tests That Distinguish Between Bacterial and Viral Infections, Tests That Identify Resistant Pathogens, and Tests That Distinguish Common Clinical Entities such as Bacterial Sinusitis and Acute Bacterial Otitis Media from Illnesses with Similar Manifestations for Which Antimicrobials Are Not Beneficial.			
CDC	Rapid detection of MRSA colonization to reduce spread within hospitals	This project assesses the benefit of using a rapid test to identify MRSA colonization and using this early information to institute appropriate infection control measures to decrease the spread of MRSA in high-risk hospital areas. Outcomes will be measured by determining prevalence and incidence of MRSA after implementation of the rapid test.	Protocol under review.
Action Item #34: Identify Economic and Other Barriers in the Health Care System (e.g., Reimbursement Policies by Third Party Payers, Managed Care Practices, Cost Considerations, Empiric Treatment Recommendations, etc.) to Diagnostic Testing That Promotes Appropriate Use of Antimicrobials. Develop Recommendations That Remove Disincentives or Promote Incentives to Such Testing.			
DVA	Laboratory accreditation	The VHA currently participates in surveys by the College of American Pathologists and all VHA laboratories are appropriately credentialed.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #35: In Collaboration With Professional Societies, Industry, Health Departments, And Other Stakeholders And Partners, Develop Guidelines for Clinicians And Clinical Microbiology Laboratories To Address Appropriate Specimen Collection, Interpretation, And Reporting Of Susceptibility Tests, And Use Of In-Office Tests For Infection.			
CDC	National laboratory system demonstration projects	These projects promote linkages and coordination between State Public Health and clinical microbiology laboratories to optimize laboratory practice, in collaboration with medical societies and other stakeholders. AR is a major focus area. Example: In one project, the State of Washington developed and distributed a survey of laboratory practices related to antimicrobial susceptibility testing (AST) and is now providing training in quality control for AST testing through a teleconference and a train-the trainer program on use of the NCCLS guidelines. The survey will then be readministered to measure changes in practice and use of the guidelines.	CDC-funded demonstration projects underway in 5 states.
CDC	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).	See Action Item #26 (State-based multifaceted interventions for clinicians and patients to promote the appropriate use of antibiotics for outpatient upper respiratory infections).
CMS	National pneumonia project	This CMS project addresses prevention of pneumonia and promotes appropriate diagnostic testing and antibiotic treatment for patients who are hospitalized because of pneumonia. It specifically promotes the use of influenza and pneumococcal vaccines, the timely collection of blood cultures, and the use of antibiotics that are consistent with published recommendations, including those of CDC.	Operational in all 50 states since 1999.
Action Item #36: In Collaboration with Professional Societies, Industry, Health Departments, and Other Stakeholders, Develop Guidelines That Address the Use of Clinical Microbiology Laboratories for Use by Health Care Delivery Organizations.			
Action Item #37: Promote the Increased Performance of Direct Examination of Microbiological Specimens (e.g., by Gram Stain or Other Rapid Method) in Circumstances Where Appropriate, Clinically Relevant, and Reliable Information Can Be Garnered, as Readily Available Point-of-Care Diagnostic Test. This Step Will Require Working Within the Framework of the Clinical Laboratory Improvement Amendment (CLIA) Regulations and Involving Medical Education And Health Care Delivery Organizations.			
CMS	See Action Item #26 (Prevention of Antimicrobial Resistance in Skilled Nursing Facilities).	See Action Item #26 (Prevention of Antimicrobial Resistance in Skilled Nursing Facilities).	See Action Item #26 (Prevention of Antimicrobial Resistance in Skilled Nursing Facilities).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #38: Identify Factors That Promote Transmission of Drug-Resistant Pathogens in Healthcare Facilities, in Extended Care Facilities, and in Community Settings, Including Daycare Centers in the Community at Large. These May Include Characteristics of the Facilities and of the Populations They Serve.			
CDC	Antimicrobial resistance in*Staphylococcus aureus* and *Streptococcus pneumoniae* among Alaskan natives	CDC is conducting surveillance and evaluation of prevention and control measures for MRSA skin infections, community-wide surveys for carriage of penicillin-nonsusceptible *Streptococcus pneumoniae*, and surveys on antimicrobial drug use. These activities will provide knowledge of MRSA prevalence and effectiveness of prevention measures, assist with the development of treatment guidelines for community-onset MRSA infections, assess the effect of the new pneumococcal vaccine on resistant pneumococcal infections, and assess the effect of education on appropriate antimicrobial agent use in Alaska.	Ongoing.
CDC	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).	See Action Item #39 (Centers of Excellence in Healthcare Epidemiology).
	See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP).	See Action Item #63 (The Chicago Antimicrobial Resistance Project CARP).
CDC	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).	See Action Item #63 (The Wisconsin Antibiotic Resistance Network).
**** TOP PRIORITY **** **Action Item #39: Evaluate the Effectiveness (Including Cost-Effectiveness) of Current and Novel Infection-Control Practices for Health Care and Extended Care Settings and in the Community. Promote Adherence to Practices Proven To Be Effective.**			
CDC	Centers of excellence in healthcare epidemiology (prevention epicenters)	Academic medical centers conduct research to improve infection control practices. Current projects address prevention of infections related to central vascular catheters and surgical site and bloodstream infections. A substantial proportion of these infections are drug-resistant. Reduction of these infections would also reduce antimicrobial use in healthcare settings, thus decreasing the environmental pressure favoring development and spread of resistant infections.	Awarded funds to 7 academic medical centers for research projects in FY 2001.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	MRSA prevalence in patients with end-stage renal disease, healthcare workers, and their household contacts	Infection with MRSA is often preceded by colonization. Although most individuals who are colonized do not develop disease, carriers can spread the organism to individuals at high risk for infection. This project measures the prevalence of, and risk factors for, MRSA colonization among high-risk patients, healthcare workers, and their household contacts and follows outcomes prospectively for MRSA-colonized individuals and selected controls. The data will be used to evaluate current infection control strategies and help design improved infection control measures to prevent the spread of MRSA.	Awarded funds to universities in FY 2001.
CDC	See Action Item #63 (comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities.	See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities.	See Action Item #63 (Comprehensive Demonstration Project: Building Regional Coalitions to Prevent Methicillin-Resistant *Staphylococcus aureus* (MRSA) in Healthcare Facilities.
DVA	Outcome effectiveness: tuberculosis, legionella	The Infectious Diseases Program Office continues to evaluate impact on infection control and educational efforts to prevent healthcare-associated and community-based infections in the veteran population served. Specific reference can be made to the VA program to combat tuberculosis and multidrug-resistant tuberculosis as a program in which intervention was defined and outcome assessed by using statistical analysis to provide objective outcome data.	Ongoing. Roselle GA, Danko LH, Kralovic SM, Simbartl LA, Kizer KW. Tuberculosis in the veterans healthcare system: a six-year review and evaluation of programme effectiveness. Epidemiol Infect. (2000), 125, 315-323. Roselle GA, Danko LH, Kelly AA, Simbartl LA, Kralovic SM. Legionella in the Department of Veterans Affairs Veterans Health Administration (VHA): the outcome of intervention over eight years. Abstract presented at the 39th Annual Meeting of the Infectious Diseases Society of America, October 25-28, 2001, San Francisco, CA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #40: Evaluate the Cost-Effectiveness and Impact on Patient Care and Drug Resistance of Medical Devices That Incorporate Anti-Infective Compounds To Prevent Infection (e.g., Anti-Infective Urinary Catheters and Prosthetic Heart Valves). Where Appropriate (e.g., Shown To Be Effective and Not Induce Resistance), Encourage the Clinical Use of These Devices.			
AHRQ	Making healthcare safer: a critical analysis of patient safety practices	Systematic literature review by Evidence-based Practice Center.	Shojania KG, Duncan BW, McDonald KM, Wachter RM, eds. Making health care safer: a critical analysis of patient safety practices. Evidence Report/Technology Assessment No. 43 [Prepared by the University of California at San Francisco-Stanford Evidence-based Practice Center under Contract No. 290-97-0013], AHRQ Publication No. 01-E058, Rockville, MD: Agenc for Healthcare Research and Quality. July 2001.
FDA	Devices containing antimicrobials – proposed rule	Advanced notice of proposed rulemaking: how to regulate devices which contain antimicrobial agents in light of public health concerns regarding AR.	Moratorium on rulemaking—awaiting clearance.
FDA	Devices containing antimicrobials – draft guidance	Draft guidance document for industry: how CDRH intends to regulate devices containing antimicrobial drugs, and what information regarding efficacy and resistance CDRH wants t see in premarket applications (interim until rulemaking is completed)	Draft circulated inside Office of Device Evaluation, February 2002.
FDA	Standards development seminar	Standards development: seminar to gather information from experts on developing test methods that should/could be used to demonstrate efficacy of antimicrobial agents on devices for use in guidance and rulemaking.	Seminar held on Dec. 3-4, 2001.
Action Item #41: Encourage the Development and Implementation of Clinical Alternatives to Those Invasive Medical Procedures and Devices That Increase the Risk of Infection in Hospitals and Other Health Care Settings, e.g., Substitutions of Transcutaneous Monitoring of Blood Oxygen Levels of Indwelling Catheters.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #42: Evaluate the Benefits and Risks of Incorporating Antimicrobial, Disinfectant, or Antiseptic Chemicals into Consumer Products (e.g., Soap, Toys, Kitchen Utensils, Clothes, Paints, Plastics, and Film Preservatives) and of Applying Disinfectants and Sanitizers to Hard, Non-porous Surfaces such as Food-Contact Surfaces, Hospital Premises, Bathrooms, etc. Consider Whether They Have Any Efficacy in Reducing and/or May Play a Role in Promoting Drug Resistance.			
EPA	Antimicrobial pesticide products: evaluation of potential role in promoting resistance to themselves and/or to drugs	(1) Determine whether there is any reasonable likelihood, based on current scientific data/information, that use of antimicrobial pesticide products results in the development of microbial resistance to either the pesticide products themselves or to human or animal drugs. (2) If it is found that there is, in fact, a reasonable likelihood that antimicrobial pesticide products play a role in resistance development, devise data requirements and data generation guidelines that will allow the Agency (EPA) to assess risks in this area.	Scientific literature search and review under way, with anticipated completion in early 2002. Potential "next steps," e.g., workshop, development of data requirements, etc., will depend on the findings of the literature search/review.
Action Item #43: Conduct a Public Health Campaign To Promote Hand Hygiene and Other Hygienic Practices, as well as Other Behaviors That Prevent the Transmission of Infectious Organisms, in Collaboration with Professional Societies and Stakeholders. This Campaign May Be Coordinated with the Public Health Education Strategy To Promote Appropriate Antimicrobial Use Described in Action Item #25: Prevention and Control.			
Action Item #44: Facilitate and Support the Activities of Infection Control Programs in Health Care Settings as a Component of Medical Care. Promote Infection Control Education at all Stages of Training and Practice for all Health Care Workers Who Have Contact with Patients.			
CDC	Division of Healthcare Quality Promotion (DHQP), National Center for Infectious Diseases (NCID)	DHQP, formerly known as the Hospital Infections Program, has in its mission surveillance, applied research, and prevention and control of infections in healthcare settings.	Numerous ongoing projects in collaboration with partners.
CMS	See Action Item #24 (Rural Antibiotic Decision-support and Resistance Project [RADAR]).	See Action Item #24 (Rural Antibiotic Decision-support and Resistance Project [RADAR]).	See Action Item #24 (Rural Antibiotic Decision-support and Resistance Project [RADAR]).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DVA	Educational activities since January 2001: A. Department of Veterans Affairs Occupational Safety and Health Conference, Las Vegas, NV, August, 8, 2001. B. Department of Veterans Affairs Occupational Safety and Health Conference, Las Vegas, NV, August, 9, 2001. C. Emerging Pathogens Satellite Broadcast, September 5, 2001 D. Infomercials taped and aired on VA Knowledge Network. Viewed by VHA employees.	Conference Speakers: A. Employee Health: Vaccine and PPD Issues. Speaker: Gary A. Roselle, M.D. B. Emerging Infectious Diseases. Speaker: Stephen M. Kralovic, M.D. C. Part 1 – Tuberculosis. Part II – Implementation Thoughts and the Future. Presenter: Gary A. Roselle, M.D. D. 2-3 minute "infomercials" covering issues relating to influenza, PPD's and bloodborne pathogens.	The VHA is currently in the forefront of infection control programs in the healthcare settings in the U.S. This includes national guidance, educational activities, and current financial support of the program nationwide. It is anticipated that such activities will continue, particularly because of the more recent emphasis on patient safety and infection control as part of an overall safety program to prevent excess infections in the healthcare setting.
Action Item #45: Support Ongoing Public Health Education Campaigns on Food Safety, such as FDA and USDA's Fight BAC Program, Whose Aims Are To Educate Food Producers, Retailers, and Consumers About Food Safety Practices That Reduce Foodborne Infections (Including AR Infections).			
Action Item #46: Educate the Public About the Merits and Safety of Irradiation as One Tool To Reduce Bacterial Contamination of Food.			
Action Item #47: Support Community-Based Programs That Promote and Facilitate Availability of Recommended Vaccinations for Adults and Children.			
CDC	National Immunization Program (NIP)	NIP's mission is to reduce disease and disability from diseases that can be prevented through immunization.	Numerous ongoing projects support state and community-based programs that promote vaccination and provide vaccines.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #48: Identify Vaccines Useful in Preventing Drug-Resistant Infections and Reducing Antimicrobial Drug Use and Evaluate Novel Methods For Improving Coverage with These Vaccines.			
CDC	Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant *Streptococcus pneumoniae* (DRSP)	A 7-valent conjugate vaccine for *Streptococcus pneumoniae*, licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. Three CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections. One project is a case-control study of vaccine effectiveness in preventing invasive infections in children in 9 Emerging Infections Program areas in which population-based active surveillance is conducted. The second project assesses impact on nasal colonization of children living in Anchorage, Alaska, through annual culture surveys. The third is a community-wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and non-vaccinees. Data from these study will be used to evaluate vaccine recommendations in the U.S. Decision makers in other countries will use this data to determine if pneumococcal conjugate vaccine should be used.	Ongoing; data collection in progress.
CMS	See Action Item #35 (National Pneumonia Project).	See Action Item #35 (National Pneumonia Project).	See Action Item #35 (National Pneumonia Project).
DVA	Improve use of vaccines related to prudent use of antibiotics	Department of Veterans Affairs, Veterans Health Administration Directive 2001-053. Influenza Vaccine – Recommendations for 2001-2002. Published and placed on VA Intranet Web site August 28, 2001. Infomercials were aired on VA Knowledge Network regarding influenza vaccine. Performance Measurement Program, FY 2001 and FY 2002 VHA Performance Measurement System Technical Manuals list Influenza Immunization and Pneumococcal Immunization as Preventive Care Quality Performance Measures, with specific recommendations for these immunizations for Nursing Home Care Units within the VHA system.	The VHA is already in the forefront of immunization practices as is evidenced by the pneumococcal and influenza vaccine usage rates compared to the national averages. In addition, influenza vaccine use increases each year in the VHA as emphasis on this program continues. Therefore, this action item is already under way and will continue to be an area of emphasis area for the DVA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #49: Evaluate the Nature and Magnitude of the Impact of Using Various Antimicrobial Drugs as Growth Promotants in Different Species, Using Current Animal Husbandry Practices. Use This Information To Assist in Risk-Benefit Assessments of Such Use.			
CDC	See Action Item #50 (Reducing resistant bacteria in food animals).	See Action Item #50 (Reducing Resistant Bacteria in Food Animals).	See Action Item #50 (Reducing Resistant Bacteria in Food Animals).
Action Item #50: Conduct Additional Research To Further Define the Effects Of Using Various Veterinary Drugs on the Emergence of Resistant Bacteria That Infect or Colonize Food Animals of Different Species, Using Various Animal Husbandry Practices. Identify Risk Factors and Preventive Measures to Humans.			
CDC, FDA	Reducing resistant bacteria in food animals	Projects assess the impact of antibiotic use in swine and cattle, develop alternatives to the use of antimicrobial drugs as growth promotants, and evaluate new practices to reduce resistant bacteria in food animals.	Awarded cooperative agreements to 4 schools of veterinary medicine (2 for studies in dairy cattle, 2 in swine).
Action Item #51: Conduct Epidemiologic And Laboratory Studies To Assess the Risk of Development and Transfer of Resistance Related to The Use of Antimicrobial Drugs in Food and Non-Food Plants, and Identify Risk Factors and Potential Preventive Measures.			
CDC	Antibiotics used as pesticides in orchards	Apple and pear orchard farmers have used streptomycin to control the plant disease fireblight, a bacterial infection caused by *Erwinia amylovora*, since the 1950s. After years of streptomycin use, streptomycin-resistant strains of *E. amylovora* developed. Farmers now use oxytetracycline in *E. amylovora* resistant areas to control fireblight. In this pilot study involving 4 orchards in 3 states, fruit is tested to determine whether human pathogens, including antimicrobial-resistant organisms, are present in orchards and whether antibiotic residues are potentially reaching the food supply.	Completed specimen collection; testing and data analysis in progress.
CDC	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).	See Action Item #55 (Assessment of the off-farm transport of waste-associated chemical and microbial constituents present on swine feeding operations).
CDC	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).	See Action Item #55 (Sampling for Antibiotics in agricultural river basin).
CDC	See Action Item #55 (Evaluation of the impact of flooding on water quality and human health indicators).	See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators).	See Action Item #55 (Evaluation of the Impact of Flooding on Water Quality and Human Health Indicators).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #52: Develop Rapid Tests For Inspecting Fresh Commodities Like Fruit For Evidence Of Contamination With Bacteria That Are Resistant To Antibiotics.			
FDA	Rapid methods development	Develop rapid methods for the identification of foodborne pathogens in animal feed.	Extramural contract with U. of Tenn. Awarded.
Action Item #53: Evaluate the Effect of Current Food Processing and Distribution Methods on the Emergence and Spread of Drug-Resistant Organisms.			
Action Item #54: Identify and Evaluate New Food Pasteurization Strategies.			
Action Item #55: Assess the Risk of AR Emergence and Spread due to Environmental Contamination by Antimicrobial Drugs or by Resistant Bacteria in Animal and Human Waste. Collect Information on Whether Environmental Contamination by Antimicrobial Drugs Can Lead to the Development of Resistance in Bacteria That Live in Soil or Water.			
CDC	Assessments of the off-farm transport of waste-associated chemical and microbial constituents present on swine-feeding operations	Soil and water samples are being assessed in the vicinity of a large farm to determine whether selected chemical and microbial constituents found in swine manure are traveling from agricultural fields onto which swine manure is applied into the local environment.	Completed specimen collection; analysis pending.
CDC	Sampling for antibiotics in an agricultural river basin	Sample and analyze water and bed sediment from streams in an agricultural river basin (containing livestock and crop farms) for antibiotics, nitrogen, and microbes and their antimicrobial susceptibilities.	Completed specimen collection; analysis pending.
CDC	Evaluation of the impact of flooding on water quality and human health indicators	Assess possible chemical and microbial contamination of surface and drinking well water in two counties that experienced flooding. This assessment includes (1) the exploration of the association between presence of concentrated animal feeding operations and levels of environmental contamination in surface, estuarine, and well water and (2) investigating the presence of human pathogens and their antimicrobial susceptibility as an indicator that may result from environmental contamination of surface and well water.	Specimen collection in progress.
Action Item #56: Assess the Impact of Antimicrobial Use in Companion Animals (Pets) on Colonization and Infection with Drug-Resistant Organisms in The Animals and Their Humans Household Contacts.			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #57: Work with Veterinary and Agricultural Communities To Help Educate Users of Veterinary and Agriculture Antimicrobials About AR Issues, and Promote the Implementation and Evaluation of Guidelines That Address These Issues.			
CDC, FDA, USDA	Liaison with American Veterinary Medical Association Steering Committee on Antimicrobial Resistance	Participate in committee activities, including development of prescribing principles and educational programs.	The committee developed General Principles for Judicious Therapeutic Use of Antimicrobial (1998), which were then adapted by species groups for their membership, to date including swine (1999), poultry (2000), bovine (2000), feline (2001), and equine (2001). Implementation is promoted through educational programs and a computerized veterinary decision support system, which is under development.
CDC	Development of model veterinary school curriculum to promote appropriate antimicrobial drug use	A curriculum is being developed in collaboration with partners that will be offered to veterinary schools.	Initiated discussions with partners re optimal content and structure.
FDA	Education/outreach	Outreach to consumers.	Public meeting with consumer groups planned for late April 2002.
FDA	Education/outreach materials	Develop outreach material on judicious use targeted to veterinarians.	Ongoing activity. Contract awarded with the American Veterinary Medical Association to develop the guidelines. Guidelines received and from these, videotapes and brochure produced for veterinary practitioners. 1) Published 4 booklets that explain prudent use principles in depth for beef, dairy, swine and poultry veterinarians and sent the appropriate booklet to food animal practitioners. 2) Produced 2 videotapes to be used at meetings and veterinary medical schools to introduce the prudent drug use principles.
**** TOP PRIORITY **** **Action Item #58: In Consultation with Stakeholders, Refine and Implement the Proposed FDA Framework for Approving New Antimicrobial Drugs for Use in Food-Animal Production and, When Appropriate, for Re-Evaluating Currently Approved Veterinary Antimicrobial Drugs.**			
FDA	Drug categorization	Develop an approach for how to evaluate drugs as to their importance in human medicine for use in animal drug premarket application requirements for use in CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	Recommendations from CDER incorporated into the pre-approval strategy.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Fluoroquinolones	Withdraw approval of fluoroquinolones for use in poultry	Sarafloxacin voluntarily withdrawn April 30, 2001; hearing requested for enrofloxacin. Notice of Hearing published February 20, 2002.
FDA	Risk assessment	Risk assessment: Conduct an analysis of the relationship between emergence of streptogramin-resistant *Enterococcus faecium* (Synercid) in humans and use of streptogramins (virginiamycin) in food-producing animals.	Draft risk assessment for distribution and public comment by Fall 2002.
FDA	Pathogen load	Develop guidance relating to antimicrobial drug effects on pathogen load and incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	Literature review published on CVM Web site May 2001. Veterinary Medicine Advisory Committee meeting held Janua 22-24, 2002.
FDA	Microbiological safety requirements	Develop pre-approval requirements for microbiologic safety regarding the use of antimicrobial agents in food-producing animals. Incorporate into CVM's guidance for industry on the strategy for ensuring the safety of new animal drugs with regard to their microbiologic effects on bacteria of human health concern.	Draft guidance to be completed Summer 2002; public meeting following publication of the guidance.
FDA	Antimicrobial use in food-producing animals	Develop rulemaking relating to annual reports of use and quantity of antimicrobial drugs marketed for food animals	Participated in WHO expert consultation on monitoring drug use in September 2001. Developing draft proposed rule and guidance.
FDA	Framework document	Refine the Framework Document and incorporate the concepts into guidance for industry on a strategy for assuring the safety of new animal drugs with regard to their microbiological effects on bacteria of human health concern.	Comments from public meetings and submitted to the Framework Document have been incorporated into guidance; small, outreach meetings held with stakeholder groups throughout 2001 for additional input.
Action Item #59: Strongly Encourage Involvement of Veterinarians in Decisions Regarding the Use of Systemic Antimicrobial Drugs in Animals, Regardless of the Distribution System Through Which the Drug Is Obtained (e.g., Regardless of Whether a Prescription Is Required To Obtain the Drug).			
FDA	Educational materials	Develop outreach materials on judicious use targeted to food animal producers.	Based on the information developed for veterinarians, FDA developed and printed booklets for swine producers and poultry producers, written with less technical language. Have contracted with specialists to write booklets for dairy and beef producers. These booklets should be printed and distributed some time late Fall 2002.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	AR use by veterinarians	Develop a Web-based decision support system for use by veterinarians to select and use antimicrobial agents appropriately.	Provided funding for development of Veterinary Antimicrobial Decision Support System; 5 year contract awarded late 2001
Action Item #60: Evaluate the Potential Impact of Making All Systemic Veterinary Antimicrobial Drugs Available by Prescription Only.			
Action Item #61: Convene an Expert Group To Consider How To Incorporate AR Issues into Regulations Governing the Registration and Use of Antimicrobials and Antibiotic Pesticides. Invite External Experts, Stakeholders, and the Public To Provide Input.			
Action Item #62: Establish an Ongoing Mechanism To Obtain Periodic Input from External Experts on AR Issues. This Process Will Include Ensuring Input from Stakeholders and Partners (e.g., State and Local Health Agencies, the Private Sector, and the Public) in Developing and Reviewing Federal Efforts To Address Antimicrobial Resistance.			
ARHQ, CDC, DoD, DVA, EPA, FDA, NIH, USDA	Antibiotic resistance task force	Annual Progress Report and Public Meeting.	Progress report issued consisting of inventory of projects that address Action Plan items. First annual public meeting June 26, 2002, Bethesda, MD.
CDC	Board of Scientific Counselors, National Center for Infectious Diseases	Discussion of CDC activities to address antimicrobial resistance at Board meetings, including extended discussion in breakout group in 2001.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #63: Support Demonstration Projects To Evaluate Comprehensive Strategies That Use Multiple Interventions To Promote Appropriate Drug Use and Reduce Infection Rates.**			
CDC	Wisconsin antibiotic resistance network	The Wisconsin Antibiotic Resistance Network (WARN) is a statewide program to reduce antibiotic overuse and reduce the spread of resistant bacteria that cause upper respiratory illnesses. WARN is a partnership between the State Medical Society of Wisconsin, the Marshfield Medical Research Foundation, and the Wisconsin Division of Public Health. Recent activities include antimicrobial susceptibility testing; implementation and evaluation of educational interventions for the community, health departments, and health professionals; pharmacy outreach, and economic analyses to determine intervention costs.	Ongoing: supported by CDC Cooperative Agreement through FY 2003.
CDC	The Chicago Antimicrobial Resistance Program (CARP)	CARP is a 5-year demonstration program to determine the impact of antimicrobial use and infection control interventions on the reduction of antimicrobial resistance in a healthcare delivery system. Components include developing improved methodology for interhospital and intrahospital comparisons of AR rates, computer-based surveillance of antimicrobial drug use, and interventions to improve antimicrobial drug use and prevent emerging resistance. It is hoped that the project will demonstrate methods for adherence to hand hygiene, decreases in rates of MRSA and VRE, reductions in use of broad-spectrum antibiotics and antimicrobial regimens with redundant antimicrobial spectra, and model the costs of healthcare associated infections.	Ongoing, supported by CDC Cooperative Agreement through FY 2003.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC	IMPART (Inter-Mountain Project on Antimicrobial Resistance and Therapy)	In Utah and Idaho, a project to implement and evaluate a comprehensive approach in rural communities (in both inpatient and outpatient settings) for surveillance of AR, to improve antimicrobial prescribing, to assess the environmental impact of antimicrobial drug use in agriculture and aquaculture and to evaluate potential routes of transmission of resistant bacteria to humans, and to identify novel biotherapeutic approaches to AR that have applicability to the rural setting. The information collected will be useful for other rural areas of the U.S. interested in detecting, preventing and controlling AR.	Three year grant awarded in FY 2001.
CDC	Comprehensive demonstration project: building regional coalitions to prevent methicillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities	This project in collaboration with The Pittsburgh Regional Healthcare Initiative (PRHI) supports development and implementation of a comprehensive program to reduce MRS infections in a large regional network of healthcare facilities. The PRHI has designated control of MRSA as a focus of quality improvement. The intervention plan is being developed, based on applying a process engineering technique borrowed from the automotive industry (Toyota Production System, TPS) to processes of patient care that contribute to the problem of AR. TPS teaches frontline workers how to improve the design and flow of work by immediately identifying and correcting outcomes or processe that are not those which are expected. This strategy should remove barriers to compliance with recommended prevention strategies. The prevention strategies include active and rapid identification and isolation of MRSA carriers, a customized plan for isolating and/or grouping colonized patients into cohorts, educational tools, a network multidisciplinary steerin task force, and others.	Ongoing. Pilot testing of the interventions has been initiated in 2 hospitals within the network (The University of Pittsburgh Medical Center-Presbyterian Hospital and the Pittsburgh Veterans Administration Hospital). Thirty hospitals in the Pittsburgh metropolitan area (includes 69 intensive care units) are now regularly reporting infection data to CDC, using standardized methodology, and facility-specific and aggregated region wide data are being fed back to PRHI quarterly. This system can be used to prospectively track the prevalence of MRSA among healthcare-associated infections.
CMS	See Action Item #25 (prevention of antimicrobial resistance in the outpatient setting).	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).
CMS	See Action Item #24 (Rural Antibiotic Decision-support and Resistance Project [RADAR])	See Action Item #24 (Rural Antibiotic Decision-support and Resistance Project [RADAR]).	See Action Item #24 (Rural Antibiotic Decision-support and Resistance Project [RADAR]).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CMS	National Surgical Infection Prevention Project (SIPP)	This CMS project promotes utilization of appropriate antibiotics for surgical prophylaxis and discontinuation within 24 hours after surgery. It involves collaboration with JCAHO and 16 other organizations. See www.surgicalinfectionprevention.orgfor details.	Development complete. Medicare quality improvement organizations (QIOs) begin fieldwork in August 2002.
DVA	See Action Item #39.	See Action Item #39.	.
Action Item #64: Utilize Federal Health Care Systems (e.g., DoD, DVA) as Models for AR Surveillance and Prevention and Control Activities Involving Appropriate Drug Use, Optimized Diagnostic Testing, Infection Control, and Vaccination Practice.			
CMS	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).	See Action Item #25 (Prevention of Antimicrobial Resistance in the Outpatient Setting).
DVA	See Action Item #39.	See Action Item #39.	See Action Item #39.
Action Item #65: For All Healthcare Systems for Which Federal Funds Are Provided, Identify and Promote Strategies To Establish AR Prevention and Control Activities as Part of Quality Monitoring Programs.			
DVA	Quality assurance programs	The Office of Quality and Performance's Performance Measurement Program, which supports the VHA Strategic Plan, serves as a vehicle for effecting change in a balanced fashion. The Performance Plan operationalizes the premise that better quality, access, and satisfaction are often more efficient. For example, improved rates of inexpensive pneumococcal vaccinations may result in decreased antibiot use. Immunization rates are assessed through a contract chart review system and are part of managers' performance standards, and, therefore, are used as part of the VHA qualit monitoring program. This is part of the VHA patient care culture. Excellent immunization rates in the VHA have resulted from this program.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #66: Encourage Nationally Recognized Accrediting Agencies such as The National Committee for Quality Assurance (NCQA), and the Joint Commission on Accreditation Standards That Promote Efforts To Prevent and Control AR, Including Appropriate Use, Infection Control, Vaccine Use, and Diagnostic Testing. These Standards May Draw on the Findings of Existing Data and Demonstration Programs and AHRQ Evidence-Based Practice Centers.			
AHRQ	Ongoing development and evaluation of HEDIS M+A15measures+A50	Grant to Harvard University for a rigorous and broad evaluation of HEDIS 3.0 specifically: 1) evaluate the new "reporting set" measures in HEDIS 3.0 and a subset of the original "reporting set" measures with respect to their relevance for users, the soundness of the science that underlies them, and the feasibility of implementing them; 2) develop complete operational specifications for a subset of "testing set" measures that are particularly strong candidates for the next version of HEDIS; and 3) evaluate the "testing set" measures that might be used in the next version of HEDIS with respect to their relevance, scientific soundness and logistic feasibility.	Based on these analyses, refinement of specific measures will be suggested and important problems will be identified with individual indicators to guide decisions about whether to include these indicators in subsequent versions of HEDIS. This work is proposed as part of a general strategy and method for developing and refining measures such as HEDIS in the future.
CMS	National Surgical Infection Prevention Project (SIPP)	This CMS project promotes utilization of appropriate antibiotics for surgical prophylaxis and discontinuation within 24 hours after surgery. It involves collaboration with JCAHO and 16 other organizations. See www.surgicalinfectionprevention.orgfor details.	Development complete. Medicare quality improvement organizations (QIOs) begin fieldwork in August 2002.
Focus Area III: Research			
Action Item #67: Additional Research, Including High Risk and High Payoff Research in Nontraditional Fields, Is Needed.			
CDC	Antimicrobial resistance mechanisms of*S. pneumoniae* (Alaska)	Use of PCR methodologies to rapidly screen*S. pneumoniae* isolates for genetic determinants of resistance; monitoring th emergence, spread, persistence, and decline of multidrug-resistance organisms by molecular-based typing capabilities to include multilocus sequence typing (MLST).	Ongoing.
FDA	Multidrug-resistant TB	Research: mechanisms of resistance in multidrug- resistant tuberculosis.	Identified genetic mechanisms for multiple mechanisms of drug resistance in*M. tuberculosis.*

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Role(s) of mutators in natural populations	Genetic mutators that mutate are present in all bacterial populations. A murine infection model was used to determin if mutator subpopulations of *Salmonella enteritidis* can promote antibiotic resistance in natural populations. Competitive infection experiments showed that mutators overtake populations of bacteria during the course of infection.	Funded FY 1999-2000 by Office of Science. Completed.
FDA	Persistence of mutators in the presence of antibiotic	While both mutator and nonmutator cells of *Salmonella enteritidis* persist in the livers and spleens of infected C57Bl/10 mice, mutator cells are less susceptible than non-mutators to the antimicrobial activity of a fluoroquinolone antibiotic administered after infection. However, mutation to antibiotic resistance does not account for the persistence of mutators in the presence of antibiotic.	Ongoing; funded by Office of Science, FDA.
FDA	Surveillance of *Shigella*	*Shigella spp* are significant contaminants in the food supply. A yearly surveillance of antibiotic resistance phenotypes in outbreak strains of *Shigella* is conducted to determine if the hazard of these foodborne contaminants has increased.	Ongoing; base funds.
FDA	Virulence of MDR *Salmonella*	The frequency of multidrug-resistant (MDR) *Salmonella typhimurium*, including DT104, has increased as those organisms have contaminated the food supply. A collection of MDR outbreak strains is being tested to determine if these strains show increased virulence in animal models.	Ongoing; base funds.
NIH	Innovative approaches for combating antimicrobial resistance	A proposed new initiative to stimulate novel and innovative research, including high risk and high payoff studies in nontraditional fields, to acquire a better understanding of the factors affecting the development of resistant pathogens and spread of resistance genes, in order to direct actions to diagnose, control, and treat AR.	Concept approved by NIAID Council January 17, 2002, request for applications under development, anticipated release May 2002.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Exploratory/developmental grants: technology applications to NIAID-funded research	A new solicitation for exploratory/developmental (R21) grant applications that facilitate the use of innovative/emerging technologies to currently funded research projects related to the study of infectious diseases (bacterial, viral, fungal, and parasitic), diseases caused by category A agents of bioterrorism, HIV/AIDS, basic immunology, and immune mediated conditions. This R21 mechanism is designed to capitalize on scientific opportunities that would augment the value of the project and may not have been available at the time of submission of the parent grant.	New program announcement (PAS-02-031) released December 5, 2001.
NIH	Investigator-initiated small research grant award program announcement	The R03 award supports small research projects that can be carried out in a short period of time, with limited resources. This solicitation extends its use to unsolicited applications in addition to its use in individual Requests for Applications (RFA) and Program Announcements (PA). This is an important mechanism for attracting new investigators to a field of study and providing sufficient support to allow development of preliminary data that will enable successful long-term funding.	New Program Announcement (PA-02-038) released on December 12, 2001.
NIH, DoD	Biotechnology Engagement Program (BTEP)	The BTEP Program is an attempt by the U.S. government to engage former Soviet Union scientists that were engaged in biowarfare research to refocus on issues of mutual benefit. DMID Program staff oversee a U.S. – Russian Collaborative TB research new project initiated in 2001 with Professor A. Ilyichev of Vector in Novosibirsk entitled, "Drug resistant tuberculosis in Western Siberia." NIGMS staff oversee, "Molecular epidemiology and antibiotic resistance of bacterial infections in Georgia" in collaboration with Lela Bakanidze of the National Center for Disease Control of Georgia.	Collaboration ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Investigator initiated grants mechanisms (R01)	NIH funds a diverse portfolio of grants to study AR in major viral, bacterial, fungal, and parasitic pathogens. Projects include basic research into the disease-causing mechanisms of pathogens, host-pathogen interactions, and the molecular mechanisms responsible for drug resistance, as well as applied research to develop and evaluate new or improved products for disease diagnosis, intervention, and prevention.	Ongoing.
NIH	Small Business Innovation Research and Technology Transfer Grants Program (SBIR/TTGP)	The SBIR/STTR program is an omnibus solicitation established under federal law that seeks to use small business to stimulate technological innovation, increase the participation of small business in federal R&D, and to increase private sector commercialization of technology development through Federal R&D. The annual set-aside for agencies with extramural research budgets over $100M is 2.5%.	Ongoing solicitation.
NIH	Scientific Advance: Pathogenesis of meningitis/emergence of new resistance in pneumococcus	Dr. Tuomanen mapped a pathway for how bacteria commit suicide and how antibiotics need this pathway to work well. A death peptide made by the pneumococcus triggers its suicide and represents a new class of antibiotics. Mutations in the death pathway result in bacteria that can no longer be killed, even by the last line drug, vancomycin. This is called tolerance. It is now known that such mutations exist in up to 20% of pneumococci circulating in the general community, meaning that 2-4% of pneumococcal infections will not respond to antibiotics.	Henriques Normark B, Novak R, Ortqvist A, Kallenius G, Tuomanen E, Normark S: Clinical isolates of *Streptococcus pneumoniae* that exhibit tolerance to vancomycin. Clin. Infect. Dis. 32(4):552-8, 2001. Grant # : R01AI27913 and R01AI39482. Principal Investigator : Elaine Tuomanen Institution : St. Jude Children's Research Hospital, Memphis, TN

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Regulatory pathway identified that controls resistance to the beta-lactamase class of drugs in *Staphylococcus aureus*	Successful implementation of antibacterial therapy has become increasingly difficult because of widespread AR. NIH-supported researchers identified a regulatory pathway that controls resistance to beta-lactamase antibiotics (antibiotics structurally related to penicillin) in *Staphylococcus aureus*. Specifically, they discovered that, in the presence of the antibiotic, resistance is modulated in a multistep pathway involving at least 2 proteins, a "DNA-binding repressor protein" and a "sensor-transducer protein" that interact to turn genes on and off and cause other protein to be made. Understanding the fundamental processes involved in AR within microbes forms an important basis for the development of prevention and treatment interventions.	Ongoing: Zhang, HZ, Hackbarth, CJ, Chansky, KM, Chambers, HF: A proteolytic transmembrane signaling pathway and resistance to beta-lactams in *staphylococci*. Science 291:1962-1965, 2001. Grant 3: R01AI46610. Principal Investigator: Henry F. Chambers. Institution: University of California, San Francisco.
NIH	Scientific Advance: An acquired and a native penicillin binding protein cooperate in building the cell wall of drug-resistant staphylococci.	Scientists now have a new understanding of the process that staphylococcal bacteria use to become resistant to penicillin-like antibiotics. Staphylococci which are responsible for serious diseases such as toxic shock, skin infections and a variety of healthcare-associated infections have been shown to utilize two proteins in overcoming the effects of common antibiotics in the beta-lactam class of drugs. These drugs attack proteins called penicillin-binding proteins (PBP), used by some bacteria to construct their protective walls. The methicillin-resistant staphylococcal strains have acquired a form of PBP that binds poorly to penicillin. Researcher have shown that the acquired PBP must work together with a native form of the protein to construct the cell wall in the presence of penicillin-like antibiotics, shedding new light on this process. The discovery may provide researchers with new drug targets for resistant infections.	Pinho, MG, de Lencastre, H, Tomasz, A: An acquired and a native penicillin-binding protein cooperate building the cell wall of drug-resistant staphylococci. Proc. Nat. Acad. Sci. 98(19):10886-10891, 2001. Grant #: R01AI45738 Principal Investigator: Alexander Tomasz Institution: Rockefeller University. New York.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Effect of antibiotic therapy on the density of vancomycin-resistant enterococci (VRE) in the stool of colonized patients	Colonization and infection with VRE have been associated with exposure to antibiotics that are active against anaerobic bacteria. A 7 month prospective study was conducted of 51 patients colonized with VRE. The density of VRE in stool of these patients was examined during and after several different antimicrobial drug treatments. It was found that with antianaerobic drug therapy a high density of colonization with VRE occurred. Among patients given antibiotics with minima antianaerobic activity, VRE decreased. Findings suggest tha selecting antimicrobial drugs that do not act on anaerobic bacteria can significantly decrease VRE colonization in patients.	Donskey, CJ, Chowdhry, TK, Hecker, MT, Hoyen, CK, Hanrahan, JA, Hujer, AM, Hutton-Thomas, RA, Whalen, CC, Bonomo, RA, Rice, LB: Effect of antibiotic therapy on the density of vancomycin-resistant enterococci in the stool of colonized patients. New Eng. J. Med. 343:1925-1932, 2000. Grant #: R01AI45626 Principal Investigator: Louis B. Rice Institution: Case Western University. Cleveland, OH
USDA	Poultry: A food animal model for following antimicrobial resistant*Enterococci*	There is continued concern about the use of antibiotics as growth promoting agents in food animals and the potential for development of antibiotic resistance in human pathogens. The long term goal of this study is to understand the processes involved in the development and spread of resistance in gram positive bacterial flora of poultry. This study will collect microflora samples from commercial poultry farms and processing/slaughter plants for one year. The farms will have one house using growth promoting antibiotics throughout the flocks' life and one house with no antibiotics used. Comparisons of drug resistance genes and plasmids will be made between poultry gram-positive commensals and human enterococci. The human samples will be obtained from the National Antimicrobial Resistance Monitoring System.	Ongoing: Hofacre, C.; Maurer, J.; White, D.; Hudson, C.; Angulo, F.; Headrick, M. University of Georgia; Department of Avian Medicine; College of Veterinary Medicine.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Prevalence, strain types and antibiotic resistance of *Campylobacter* in turkey grow-out farms	*Campylobacter* is a leading cause of human food-borne illness in the U.S. Transmission involved primarily poultry, although pork, beef, raw milk, and other sources have also been identified. Resistance to several antibiotics, including fluoroquinolones, commonly used for treatment of human infections, is increasing in *Campylobacter*. Extensive studies with broilers suggest that birds become colonized in the farm, usually without symptoms, and that meat becomes contaminated during slaughter and processing. This study will investigate the prevalence of *Campylobacter* in 60 turkey growout farms in Eastern North Carolina. It will evaluate the impact of distinct turkey husbandry practices in the grow-out turkey farms, and of antibiotic use for veterinary purposes, on *Campylobacter* prevalence, strain types, and antibiotic resistance profiles. The results from this study will provide a currently unavailable database on *Campylobacter* colonization, subtypes and antibiotic resistance in turkeys.	Ongoing: Kathariou, S.; Carver, D. North Carolina State University; Department of Food Science Grant 2001-35212-108.
USDA	Clonal dissemination of antimicrobial resistant *Campylobacter jejuni* and *Escherichia coli*	There is an increasing concern that antibiotic resistance in both pathogenic bacteria and in the normal flora present a risk to the public health, and reduction in the degree of antibiotic resistance is an important public health goal. The antibiotic resistant flora that appear after antibiotic exposure of cattle and other food animals may be 'new' antibiotic resistant strains originating on the farm, or may be pre-adapted strains that originated elsewhere and were transferred to the farm by animals, feed, water, wildlife, humans, or other mechanisms. The origin is important, since different origins require different control measures. For *Salmonella typhimurium*, wide dissemination of antibiotic resistant strains is the predominant process. This study will look at whether wide dissemination of antibiotic resistant strains is also important in *Campylobacter jejuni* and *E.coli* in the bovine intestine. In addition, this study will determine whether antibiotic resistant *E.coli* can be competitively displaced by non- antibiotic resistant strains.	Ongoing: Besser, TE.; Sischo, WM.; Hancock, DD. Washington State University, Department of Veterinary Microbiology and Pathology.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	AR in swine given 5 in-feed antibiotic regimens	This study is designed to measure the association between the use of five antimicrobial regimens in swine and the presence of antimicrobial resistance in human food-borne pathogens isolated from pigs on farms in the Midwest and their caretakers.	Ongoing: Barbara E. Straw, DVM, PhD Large Animal Clinical Sciences, Michigan State University.
USDA	Determinants of AR in *Escherichia coli* isolated from calves	The goals of this project are to describe the dynamics of antibiotic resistance in commensal *Escherichia coli* isolated from calves, link the patterns of resistance to management and environmental attributes, define the economics of antibiotic use, and develop educational modules to describe approaches that minimize the occurrence of antibiotic resistant bacteria.	Ongoing: William Sischo, PhD University of California, Vet Med Teaching and Research Center.
USDA	Antibiotic usage and risk factors for AR in pork production	This 3 year study is designed to determine an association between the use of antimicrobial agents in swine production and the presence of antimicrobial resistance in human foodborne pathogens isolated from slaughter pigs.	Ongoing: Bo Norby, PhD Large Animal Clinical Sciences, Michigan State University.
USDA	Antimicrobial Drug Use and the Development of Resistant Enteric Bacteria in Dairy Cattle	The objectives of this study are to 1) Determine the effect of antimicrobial treatment on the development of resistance in bacteria present in dairy cattle, 2) Develop and apply prudent antimicrobial-use guidelines specific for dairy cattle, and 3) Disseminate these guidelines to dairy producers and their veterinarians. It is expected that scientifically based interventions will be obtained and disseminated for use by veterinarians and dairy producers to address important issue of public health concern which pose a threat to their future livelihood.	Ongoing: Thomas Wittum, PhD The Ohio State University
USDA	Factors affecting the emergence of quinolone-resistant *Campylobacter* in poultry	The main goal of this project is to use an integrated approach to study quinolone-resistant campylobacters in the poultry reservoir and to establish an education and extension program on antibiotic resistance.	Ongoing: Qijing Zhang, PhD Food Animal Health Research Program, The Ohio State University.
USDA	Determination of the relationships between antibiotic resistance and virulence in *Salmonella*	Bacterial strains were obtained from clinical cases of salmonellosis and ARS found that a small group of multiple antimicrobial resistant Salmonella are capable of secreting a cytotoxin. The results demonstrate that the hypervirulent abilities of multiple antimicrobial resistant Salmonella could b due to an ability to damage cells within a host.	Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center (NAD).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Develop a fundamental understanding of the process of antimicrobial resistance in order to prevent the spread of unwanted resistant factors among the microorganisms that live normally in the gut of swine and cattle	ARS used continuous culture models of gut bacteria to determine the effect of the drug vancomycin on bacteria within the continuous culture model and within the gut of animals. Although ARS previously demonstrated that growth of certain vancomycin-resistant microorganisms was prevented in the model by the bacterial mixture, ARS found that a sub-therapeutic concentration of vancomycin in the growth media will allow these microorganisms to survive in the culture. This information will be used to determine antimicrobial dose and duration regimens that are therapeutically effective but limit the spread of antibiotic resistant bacteria, and will ultimately lead to more appropriate approaches to using antibiotics in food animal agriculture.	Ongoing: USDA-ARS: College Station, TX.
USDA	Determination of the persistence of antimicrobial resistant pathogens in the environment.	The persistence of antimicrobial resistant bacteria following the cessation of use of a given antibiotic is a problem for the development of effective intervention strategies to combat antimicrobial resistance. In collaboration with the FDA Cente for Veterinary Medicine, ARS examined the antimicrobial resistance patterns of disease causing strains of Escherichia coli from newborn pigs experiencing diarrhea. ARS found that 53% of the isolates were resistant to chloramphenicol, a broad spectrum antibiotic that has been banned for use in food animals in the United States since the mid 1980s. This information will help to determine the factors that govern the persistence of resistance genes once an antibiotic is no longer used in animal agriculture.	Ongoing: USDA-ARS College Station, TX.
USDA	Assessment of the effect of penta-resistant bacteria on virulence and/or colonization	ARS challenged broiler chicks on the day of hatch with either a sensitive or penta-resistant Salmonella typhimurium DT104 and determined that penta-resistant bacteria did not cause clinical illness in broiler chicks. However, ARS did observe a significant increase in the numbers of birds that were colonized in the penta-resistant group. In contrast to *in vitro* studies, these data indicate that acquisition of multiple resistance does affect colonization rates but may affect the numbers of bacteria that may reach the food chain.	Ongoing: USDA-ARS: Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #68: Conduct Further Government-Wide Assessments with External Input on the Scope and Composition of AR Research To Identify Research Opportunities.			
NIH	Antimicrobial strategies and cardiothoracic surgery working group	Collaboration between NIAID and NHLBI to bring scientific experts together to explore novel research and antimicrobial strategies such as vaccines and drugs for use in the prevention and treatment of infections following cardiac surgery, including complications relating to the development of AR. The group of outside experts will identify gaps and opportunities for additional research to be supported by joint Institute ventures.	Meeting held April 4-5, 2002 in Bethesda, MD.
NIH	NIAID summit on development of infectious disease therapeutics	NIAID convened a meeting to explore the role and nature of NIAID/pharmaceutical collaborations in developing therapeutics for infectious diseases, including resistant infections. The meeting objectives included determining the current and future areas of interest/activities by small and large businesses in which industry planned to proceed independently, areas in which government collaboration could facilitate pharmaceutical involvement, and infectious disease areas in which pharmaceutical companies would have no interest, even with significant government collaboration. Resource needs were also discussed.	Participants agreed that knowledge provided from basic research sponsored by NIH provides the underpinning for the development of new drugs. These activities are a major resource and should continue and be strengthened, particularly in the areas of functional genomics, mechanisms of drug resistance, and microbial physiology and ecology. http://www.niaid.nih.gov/dmid/drug/summit.htm
NIH	Pharmacologic factors in the development of drug resistant pathogenic bacteria workshop	An NIAID-sponsored interactive workshop with scientific experts from academia and industry to explore issues related to development of new drugs for resistant bacterial infections, and dosing of existing drugs to maximize efficacy and minimize resistance development. Recommendations for new NIH initiatives and interactions with industry will be sought. AR program activities will be discussed and assessed.	Scheduled for late Spring or early Summer 2002 in Bethesda, MD.
Action Item #69: Work with the Appropriate Peer Review Structures To Ensure That the Requisite Expertise Is Applied to the Review Process To Facilitate Funding of Quality AR Research.			
NIH	Bacteriology and mycology study sections	Recommendations for additional scientific reviewers with expertise in AR be added to selected study sections.	Recommendations were made, and selected reviewers with expertise in AR were added to study sections.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Outside assessment of Infectious Diseases and Microbiology Integrated Review Group (IDM IRG)	The IDM IRG review by the Expert Working Group was conducted from May – August 2001. Overall, the members of study sections in IDM were found to have strong expertise for the science reviewed and to produce high quality, fair reviews. The SRAs were deemed conscientious, hard working, knowledgeable, and competent. Issues identified in multiple study sections that need addressing are 1) the clustering of priority scores near perceived paylines, 2) a diminishing number of applications in some longstanding study sections, 3) possible inequities in treatment of new investigators acros study sections, and 4) the negative effects of streamlining/unscoring on a large number of applications.	The working group recommended that greater attention be given to priority score clustering, that greater fostering be give to young scientists and new investigators, and greater effort b expended to revitalize the few study sections experiencing diminishing numbers of applications. The recommendations are being implemented.
**** TOP PRIORITY **** **Action Item #70: Provide To the Research Community Genomics and Other Powerful Technologies To Identify Targets in Critical Areas for the Development of New Rapid Diagnostics Methodologies, Novel Therapeutics, and Interventions To Prevent the Emergence and Spread of Resistant Pathogens. Examples Include Tools Such as Microbial Genome Sequences, Information on Comparative Genomics, DNA Chip Technology, Informatics, and Assistance in the Application and Use of These Tools.**			
FDA	Genomics and Proteomics	Research in support of the use of genomics, proteomics and other powerful technologies to identify targets in critical areas for the development of new rapid diagnostic methodologies, novel therapeutics, and interventions to prevent the emergence and spread of resistant pathogens.	Established microarray group and CBER core facility (for producing and reading DNA microarray chips). Initiated several research projects related to vaccine development, AR and pathogen identification.
NIH	The tuberculosis research materials and vaccine testing contract (Colorado State University)	Through this contract, NIAID provides TB research reagents to qualified investigators throughout the world, enabling them to work with consistent, high quality reagents prepared from the highly contagious and technically demanding causative pathogen, Mtb. Starting in FY2002, this contract calls for making reagents available for functional analysis of mycobacteria. Screening potential TB vaccine candidates in appropriate animal models is also conducted through this contract.	To date, screened 170 candidates or combinations under this contract. Information and reagent request forms are available at: http://www.cvmbs.colostate.edu/microbiology/tb/top.htm

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	NIAID pathogen functional genomics resource center	Contract (N01AI15447) to support the expanded program on pathogen genomics of the NIAID, with the goal of accelerating research for the systematic understanding of the genomic information of microbial pathogens and invertebrate vectors. The center will provide tools, including relational databases, computational tools, microarrays, and proteomics reagents; and training to scientists and researchers on utilizing genomic information to understand the disease-causing characteristics of a variety of pathogens and invertebrate vectors of infectious diseases. This RFP (AI02-02) was issued in response to recommendations developed by the Blue Ribbon Panel convened by NIAID in May 1999.	Awarded contract to The Institutes for Genomic Research (TIGR) on September 27, 2001. Identified three high priority organisms identified for year one activities:*Staphylococcus aureus, Streptococcus pnuemoniae, and Salmonella typhimuriu*m, all pathogens that have developed significant AR. www.niaid.nih.gov/contract/archive/RFP0202.pdf
NIH	Sequencing of whole pathogen genomes	NIAID has made significant investment in large-scale project to sequence the genomes of medically significant bacterial, fungal, and parasitic pathogens. In addition, NIAID collaborates with other funding agencies to sequence larger genomes of protozoan pathogens such as the organism that causes malaria. A listing of currently active pathogen genome sequencing projects is available at http://www.niaid.nih.gov/cgishl/genome/genome.cfm The availability of microbial and human DNA sequences will open up new opportunities and allow scientists to examine functional analysis of genes and proteins in whole genomes and cells, as well as the host immune response and an individuals' genetic susceptibility to pathogens.	NIAID supported approximately 47 large-scale sequencing projects in FY 2001 for microbial pathogens and invertebrate vectors with publication of the complete genome sequences of *Escherichia coli* (O157:H7 strain), *Streptococcus pneumoniae* (serotype 4), *Streptococcus pyogenes* (M1 GAS), and *Ureaplasma urealyticum* (serovar 3), among others.
NIH	Infectious etiology of chronic diseases: novel approaches to pathogen detection request for applications	An RFA (AI01-004) was issued in FY2001 to solicit applications on the development of novel or improved technologies to identify and validate the role of pathogens in chronic diseases for which an infectious etiology is suspecte Areas of particular interest are studies using recent technological approaches in genomics, molecular biology, proteomics, and computational biology.	Awards anticipated in FY 2002 (http://grants.nih.gov/grants/guide/rfa-files/RFA-AI-01-004.html).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	NIAID pathogen genomics Web site (http://www.niaid.nih.gov/dmid/genomes/)	The updated NIAID genomics Web site serves as a focal point to disseminate to the scientific community current information about NIAID's microbial genomics research program and related activities, including information on funding opportunities, policies, application procedures, priorities for large-scale genome sequencing projects, press releases, and currently funded large-scale genome sequencing projects.	Currently available to the scientific community.
NIH	Sexually transmitted pathogen genomic resources	NIAID continues to provide support for databases of genomic and postgenomic information on sexually transmitted pathogens http://www.stdgen.lanl.gov/	Currently available to the scientific community.
NIH, USDA, FDA, EPA, FDA	Microbe project interagency working group	NIAID staff is participating in the Microbe Project Interagency Working Group, which developed a coordinated, interagency 5 year action plan on microbial genomics, including functional genomics and bioinformatics in FY2001 .	Ongoing collaboration (http://www.ostp.gov/html/microbial/start.htm).
NIH	Bioengineering Consortium (BECON)	BECON is a trans-NIH committee composed of representatives from each of the NIH centers, institutes and divisions, including representatives from other federal agencies www.grants.nih.gov/grants/becon/becon.htm.In FY2001, NIAID participated in two BECON program announcements that support multidisciplinary research with a focus on bioengineering to develop knowledge and/or methods to prevent, detect, diagnose, or treat disease or to understand human health and behavior. These grants allow biomedical research scientists to partner with scientists from other disciplines, including physics, mathematics, chemistry, computer sciences, and engineering, to approach current complex biological problems.	In FY 2001, NIAID funded three BRGs (R01AI48665, Gene Engineering and Combinational Biology; R01AI47427, Biosensor for Investigating a Developing Immune Response; and R01AI49541, A Microfabricated Device for Rapid Viral Genome Analysis).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Network on Antimicrobial Resistance in *Staphylococcus aureus* (NARSA)	The network includes approximately 33 basic researchers, clinical laboratories and infectious disease clinicians involved in staphylococcal AR research. NARSA supports electronic sharing of information and meeting is integrated with CDC's surveillance system on antibiotic resistance, and supports a case registry and repository of well-characterized staphylococcal isolates.	Plans are being developed for expanding the repository to include a representative panel of clinical methicillin-resistant *Staphylococcus aureus* (MRSA) isolates from a variety of disease conditions, research isolates, genome sequenced isolates, virulence and toxin-producing strains, and a broader representation of drug-resistant strains. The third annual meeting of the network took place on March 7-8, 2002. NARSA has also sponsored a staphylococcus annotation meeting in collaboration with TIGR and a community MRSA meeting in collaboration with CDC. Information concerning NARSA can be found at: (http://narsaweb.narsa.net/wwwindex.html) http://www.niaid.nih.gov/newsroom/staph.htm
NIH	Pneumococcal reference and resource laboratory	NIAID continues to support a pneumococcal reference and resource laboratory through a contract awarded to the University of Rochester. Its purpose is to develop and standardize pneumococcal assays and reference reagents, measure and quantitate antipneumococcal antibody responses, develop new pneumococcal functional antibody assays, and disseminate antigens and reagents.	Ongoing.
NIH	Brochure on NIAID's microbial genomics research program	This brochure will highlight recent accomplishments in the areas of genome sequencing of microbial pathogens and invertebrate vectors of infectious disease as well as related functional genomic activities.	To be developed and made available to the scientific community in FY 2002.
NIH	Research Center Grant, "Structural Organization and Proteomics of TB"	This global consortium, which in FY 2001 expanded to include 60 laboratories from 30 institutions in 9 countries, will determine and analyze the structures of over 400 functionally relevant Mtb proteins.	The structural and functional information will be publicly available through Web-based databases (http://www.doe-mbi.ucla.edu/TB/).

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Differences in the genomic sequence between pathogenic and non-pathogenic *E. coli*	In an effort to understand the similarities and differences between pathogenic and nonpathogenic strains of *E. coli*, Dr. Frederick Blattner and his colleagues sequenced the genome of *E. coli O157:H7* and compared it with the sequence of the nonpathogenic *E. coli K12*. They found that 70% of the genome of *E. coli O15:H7* is identical to that of the non-pathogenic strain. In addition, they found that the genome of *E. coli 015:H7* is about 30% larger than the nonpathogenic strain. This additional DNA includes genes that code for the shiga-like toxins and other virulence factors. Comparison of these and other strains of *E. coli*, will provide key evolutionary information and provide insight into disease processes. Identification of the virulence genes should help in the design of new therapies and vaccines.	Perna NT, Plunkett G 3rd, Burland V, Mau B, Glasner JD, Rose DJ, Mayhew GF, Evans PS, Gregor J, Kirkpatrick HA, Posfai G, Hackett J, Klink S, Boutin A, Shao Y, Miller L, Grotbeck EJ, Davis NW, Lim A, Dimalanta ET, Potamousis KD, Apodaca J, Anantharaman TS, Lin J, Yen G, Schwartz DC, Welch RA, Blattner FR: Genome sequence of enterohaemorrhagic *Escherichia coli O157:H7*. Nature 409: 529-533, 2001. Grant #: R01 AI44387 Principal Investigator: Dr. Frederick Blattner. Institution: University of Wisconsin.
NIH	Scientific Advance: Complete genome sequence of a virulent isolate of *Streptococcus pneumoniae*	NIAID-supported scientists have determined the complete DNA sequence of a serotype 4 isolate of *Streptococcus pneumoniae* responsible for acute respiratory infection, otitis media, pneumonia, bacteremia, and meningitis. By analyzing the DNA sequence and comparing it to that of other strains, new insights into the basic biology and pathogenicity of *Streptococcus pneumoniae* have been revealed. Genome sequence analysis identified extracellular enzyme systems for metabolism of polysaccharides and hexosamines that are potentially important for the synthesis of the capsule and the virulence of the species. 69 proteins were predicted from the DNA sequence that are likely to be exposed on the surface of the organism and may serve as possible vaccine candidates.	Tettelin H, Nelson KE, Paulsen IT, Eisen JA, Read TD, Peterson S, Heidelberg J, DeBoy RT, Haft DH, Dodson RJ, Durkin AS, Gwinn M, Kolonay JF, Nelson WC, Peterson JD, Umayam LA, White O, Salzberg SL, Lewis MR, Radune D, Holtzapple E, Khouri H, Wolf AM, Utterback TR, Hansen CL, McDonald LA, Feldblyum TV, Angiuoli S, Dickinson T, Hickey EK, Holt IE, Loftus BJ, Yang F, Smith HO, Venter JC, Dougherty BA, Morrison DA, Hollingshead SK, Fraser CM. Complete genome sequence of a virulent isolate of *Streptococcus pneumoniae*. Science 293: 498-506, 2001. Grant #: U01 AI40645 Principal Investigator : Susan Hollingshead. Institution: University of Alabama at Birmingham.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Genome sequence of *Streptococcus pyogenes*: implications for treatment and prevention	Determining the DNA sequence of*S. pyogenes* is an important advance in developing new approaches to understanding how GAS causes so many different illnesses. For example, within the 2 million DNA base pairs of the genome, scientists have found more than 40 virulence genes (genes that contribute significantly to the bacterium's ability t cause disease), half of which were previously unknown. This genetic breakthrough is expected to lead to new treatments for GAS infections and new vaccine candidates.	Ferretti JJ, McShan WM, Ajdic D, Savic DJ, Savic G, Lyon K, Primeaux C, Sezate S, Suvorov AN, Kenton S, Lai HS, Lin SF Qian Y, Jia HG, Najar FZ, Ren Q, Zhu H, Song L, White J, Yuan X, Clifton SW, Roe BA and McLaughlin R. Complete genome sequence of an M1 strain of Streptococcus pyogenes. Proc. Nat. Acad. Sci. 98: 4658-4663, 2001. Grant #: R01 AI38406 Principal Investigator : Joseph Ferretti. Institution: University of Oklahoma Health Sciences Center.
NIH	Scientific Advance: Potential novel, vaccine candidates against bacterial meningitis identified from genomic sequences	Dr. Stojiljkovic and his colleagues conducted a computer search of *N. meningitidis* and *N. gonorrhoeae* genome databases to identify new outer membrane proteins (OMP) o the bacteria and subsequently characterized the proteins and determined their distribution on the bacterial surface. Future efforts will determine the usefulness of these proteins as a vaccine candidate.	Turner PC, Thomas CE, Stojiljkovic I, Elkins C, Kizel G, Ala'Aldeen DA, Sparling PF. Neisserial TonB-dependent outer-membrane proteins: detection, regulation and distribution of three putative candidates identified from the genome sequences. Microbiology47: 1277-90, 2001. Grant #: RO1AI42870. Principal Investigator: Igor Stojiljkovic. Institution: Emory University School of Medicine, Atlanta, GA
USDA	Identification and detection of antibiotic resistance genes in intestinal bacteria	ARS developed PCR assays to differentiate among nine classes of tetracycline resistance genes (classes A, B, C, D, E, G, H, K, L) and the assays were validated by using known stock cultures. Three methods for extracting DNA from swine fecal samples were compared and a MoBio commerci kit chosen based on quantity and quality of DNA product. Culture methods for isolating tetracycline resistant bacteria from the swine intestinal tract were developed and used to analyze cecal bacteria from grower stage swine from a farm that has not used antibiotics for growth promotion purposes for at least three years. These methods will be useful to researchers and regulators for measuring antibiotic resistance and developing intervention strategies.	Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #71: Encourage Sharing of AR Data Between Industry and the Research Community, Including Genomics and Other Technologies.			
NIH	Annotation and comparison of *Staphylococcus aureus* genomes	Collaboration between NIAID, researchers and academicians studying *S. aureus*, the Institute for Genomic Research, and the Sanger Center to complete the annotation of the *S. aureus* genome. A 1 day meeting was hosted at TIGR and sponsored by the NIAID to bring together world experts to facilitate completing critical steps in sequencing, annotation, and comparison of staphylococcal strains and thus make important genomic data available to the research community.	Sequence and annotation completed and available on the TIGR, Sanger Center and NIAID Web sites.
NIH	Wyeth Ayerst *S. aureus* transcriptional profiling data	Wyeth Ayerst *S. aureus* transcriptional profiling data have been made available to the Network on Antimicrobial Resistance in *Staphylococcus aureus* program for use by the scientific community through a link on the NARSA Web site. Information concerning virulence gene regulation generated from these studies will allow pursuit of new drug and vaccine targets.	Ongoing negotiations and collaboration.
NIH	Collaboration on genomics technologies and resources	NIAID continued its agreement with the Defense Advanced Research Project Agency (DARPA) in support of genomics efforts targeted at pathogens of potential bioterrorist threat in FY 2001. Under the terms of the agreement, DARPA transferred funds to NIAID for support of large-scale genome sequencing projects for *Brucella suis*, *Burkholderia mallei*, *Clostridium perfringens*, and *Rickettsia typhi*.	Collaboration ongoing.
NIH	Newly accepted cooperative agreement awards for large-scale genome sequencing projects	New large-scale genome sequencing grants were awarded in FY 01 for: *Aedes aegypti*, *Anopheles gambiae, Brugia malayi, Coccidioides immitis, Group B streptococcus, Histoplasma capsulatum, Rickettsia rickettsii, Toxoplasma gondii, and Trichomonas vaginalis.* In addition, NIAID funded large-scale sequencing projects for *Cryptococcus neoformans* and *Schistosoma mansoni*. Consideration is given to projects based on recommendations of priorities for large-scale genome sequencing projects of a Blue Ribbon Panel convened by NIAID in May 1999.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #72: Bring New Researchers into the Field, by Utilizing Appropriate Strategies such as Training and Research Opportunities.			
NIH	Investigator initiated small research grant award	The R03 award supports small research projects that can be carried out in a short period of time with limited resources. This solicitation extends its use to unsolicited applications in addition to its use in individual Requests for Applications (RFA) and Program Announcements (PA). This is an important mechanism for attracting new investigators to a field of study and providing sufficient support to allow development of preliminary data that will enable successful long-term funding.	New Program Announcement (PA-02-038) released
NIH	Research Scholar Development Award (RSDA)(K22)	The RSDA will provide support for postdoctoral fellows who are moving to assistant professor positions in an academic institution. The purpose of the RSDA is to ease the transition to an academic position by enabling the recipient to focus on the establishment of his/her research laboratory prior to submitting applications for grant support. This is intended to establish new young investigators in needed fields, including AR.	New initiative (PAR-02-018) released November 15, 2001.
NIH	Other ongoing training and research fellowship awards	PA-00-003 Mentored Clinical Scientist Development Award (K08) PA-00-004 Mentored Patient Oriented Research Career Development Award (K23) PA-00-005 Mid-career Investigator Award in Patient Oriented Research (K24)	Important ongoing programs are fostering the development of young scientists and clinical investigators.
Action Item #73: Organize Conferences That Address Research Issues Relating to AR.			
CDC, EPA, FDA, NIH, USDA	2002 Conference on Antimicrobial Resistance: Science, Prevention, Control	Scientific conference June 27-29, 2002 in Bethesda, MD, sponsored by National Foundation for Infectious Diseases, in collaboration with CDC, EPA, FDA, NIH, USDA.	Organized conference.
AHRQ	Workshop on economics of antibiotic resistance	Conference organized by Resources for the Future at Airlie House, Virginia, April 5, 2001.	Conference proceedings in preparation.
AHRQ	Expert Meeting—The use of oral antimicrobial agents in children: remaining questions	Conference sponsored by AHRQ on treatment of otitis media in children.	Held conference on April 20, 2002.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	National Foundation for Infectious Diseases 2002 Annual Conference on Antimicrobial Resistance: Science, Prevention, Control	NFID-sponsored scientific conference to provide an interdisciplinary scientific forum to present, discuss, and address the science, prevention and control of AR to define issues and potential solutions to the problem of AR.	Scheduled for June 26-28, 2002
NIH	Antimicrobial strategies and cardiothoracic surgery working group	Collaboration between NIAID and NHLBI to bring scientific experts together to explore novel research and antimicrobial strategies such as vaccines and drugs for use in the prevention and treatment of infections following cardiac surgery including complications relating to the development o AR. The group of outside experts will identify gaps and opportunities for additional research to be supported by joint Institute ventures.	Held April 4-5, 2002, in Bethesda, MD.
NIH	Community Methicillin-Resistant*Staphylococcus Aureus* (MRSA) Meeting	The NIAID through its NARSA contract and in collaboration with CDC, sponsored an experts meeting on August 18, 2001. At this meeting experts explored the origin, definitions, natural history, and research opportunities relating to the emergence of MRSA in community settings.	Assessing future collaboration of NARSA researchers and the public health community.
NIH	DMID Program staff serve as external consultants or liaison to a variety of national and international TB-related groups.	Program staff consult and serve as liaison members to national groups, including the Advisory Council for the Elimination of Tuberculosis (ACET) and the CDC TB Clinical Trials Consortium. International activities include chairing WHO's TB Vaccine Initiative Advisory Committee (TBVIAC), STOP TB Coordinating Board, and Chair of the STOP TB Vaccine Working Group. Program staff also serve as an external advisor to an EC-supported TB Vaccine Development Cluster that is coordinated by Dr. Brigitte Gicquel of the Pasteur Institute, France, and participates in the US-Indo VAP TB Working Group.	Ongoing.
NIH	A joint meeting of the U.S.-Japan Cooperative Medical Sciences Program's TB and Leprosy Panel	A joint meeting was convened by program staff in New Orleans, LA, on July 15-17, 2001, to foster an exchange of ideas and stimulate international collaborations between U.S. and Japanese TB and leprosy investigators. For more information about this program: http://www.niaid.nih.gov/dmid/other/usjapan/DEFAULT.htm	Collaboration ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	The 1998 International Symposium for Tuberculosis Vaccine Development and Evaluation.	The DMID cosponsored the meeting where the draft "Blueprint for TB Vaccine Development'was presented to the broader research community The Blueprint Report outlines the specific steps needed to develop new, improved anti-TB vaccines. Comments from symposium participants were incorporated into a Blueprint Report. NIAID, along with CDC, USAID, ACET, and FDA, briefed Assistant Secretary of Health Dr. David Satcher on the Blueprint Report. Subsequent to the briefing, Dr. Satcher convened a trans-DHHS Task Force to oversee implementation of the Blueprint Report.	Program staff continue to represent NIH on this task force.
CDC, FDA, NIH	Workshop on fluoroquinolone antibiotics for TB	This meeting, organized by the Global Alliance for Tuberculosis Drug Development (GATB), was held in Bethesda, MD, on April 23-24, 2001. The meeting was focused on the "Role of Fluoroquinolones for Treatment of Tuberculosis. Bringing together investigators involved in all phases of TB drug development, the workshop sought to recommend a strategic approach for the GATB regarding the evaluation of fluoroquinolones for TB treatment and prevention.	The primary recommendations were to explore the clinical potential of the newer licensed fluoroquinolones with activity against Mtb (moxifloxacin, gatifloxacin, levofloxacin) and to screen for more potent and less toxic quinolones from among libraries of candidate compounds.
USDA	Meeting: Impact of antimicrobials on agriculture	USDA (Cooperative State Research, Education and Extension Service, Agricultural Research Service and Food Safety and Inspection Service) financially supported a research colloquium sponsored by the American Society of Microbiology on the impact of antimicrobials in agriculture in November 2001. This meeting of 35-40 experts provided a forum to discuss the current status, future directions and actions related to the use of antimicrobial resistance in agriculture. The report will be released in Spring/Summer 2002.	Held meeting November 2001.
USDA	Meeting: Antibiotic resistance	Dr. Mary Torrence of USDA's Cooperative State Research Education and Extension Service a half-day session on antimicrobial resistance at the annual meeting of the American Veterinary Medical Association. Nashville TN, July, 2002. The session will cover antimicrobial resistance issues ranging from the farm to the table.	To be held July 2002.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Workshop: A workshop on epidemiologic methods and approaches for food safety.	A USDA-CSREES sponsored workshop entitled, AA Workshop on epidemiologic Methods and Approaches for Food Safety - Fall 2000, included a section on antimicrobial resistance and how to improve methods and approaches to study it.	Held meeting Fall 2001. The proceedings can be obtained from the following Web site: http:\\www.unl.edu\ianr\vbs\wills\Epiconf
Action Item #74: Explore the Need To Encourage Preclinical Studies on the Toxicology, Pharmacokinetics of Novel Therapeutic Agents for the Treatment of Multidrug-Resistant Pathogens And Facilitate the Transition of Potential Products from Preclinical to Clinical Studies Leading to Development by Industry of Novel Therapeutic Agents.			
NIH	Pharmacologic factors in the development of drug-resistant pathogenic bacteria workshop	An NIAID-sponsored interactive workshop with scientific experts from academia and industry to explore issues related to development of new drugs for resistant bacterial infections, and dosing of existing drugs to maximize efficacy and minimize resistance development. Recommendations as to new NIH initiatives and interactions with industry will be sought. AR program activities will be discussed and assessed.	Scheduled to occur late Spring or early Summer 2002 in Bethesda, MD.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #75: In Consultation with Academia and the Private Sector, Identify and Conduct Human Clinical Studies Addressing AR Issues of Public Health Significance That Are Unlikely To Be Studied in the Private Sector.**			
DVA	VA research update	VA investigators have a rather extensive portfolio in antibiotic resistance research that for fiscal year 2000 identifies 23 separate funded proposals in antibiotic resistance. For FY 2001, there are 29 funded projects related to AR by DVA investigators. These funded research grants cover a wide spectrum of antimicrobial resistance issues. In addition, these do not include large clinical trials that may have impact on AR such as collaboration with the NIH-funded HIV ACTG's and pharmaceutical corporate-related research that is widespread throughout the VHA. A specific area of emphasis is transmission of resistance among organisms and spread of these organisms from person to person. Such topics as spread of resistance in nursing homes, the relationship of resistance to staffing levels, and work practices (organization) as they relate to antibiotic resistance are all part of DVA investigators' portfolios and are topics unlikely to be studied in the private sector.	Ongoing. In FY 2001, 28 projects related to bacterial resistance were underway, an increase of over 300% from 1997.
NIH	Tuberculosis Research Unit (TBRU)	The TBRU contract (N01-AI-95383), established in 1994, was re-competed in 1999 and awarded again to Case Western Reserve University. The research group continues to make progress in developing surrogate markers of disease and human protective immunity and in conducting clinical trials of potential new TB therapeutic, preventive, and diagnostic strategies. Furthermore, well-characterized clinical samples will be available for distribution to qualified investigators worldwide through a newly established repository. Activities of the TBRU are coordinated with other major organizations involved in TB research, including CDC, USAID, FDA, WHO, the Global Alliance for TB Drug Development, and interested industrial partners.	On-going: Pilot Immunology Studies (Uganda). Phase II study of rhIL-2 (Proleukin®) in HIV-noninfected Adults with Pulmonary TB (Uganda) Immunologic and Microbiologic Predictors of Response to Standard Anti-TB Treatment (Brazil)

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Bacteriology and Mycology Study Group (BAMSG)	A contract establishing a clinical studies collaborative group with the expertise to plan, design, construct, and conduct clinical studies addressing diagnosis, treatment, and prevention of serious fungal and healthcare-associated resistant bacterial infections was awarded to University of Alabama/Birmingham in April 2001. A focus will be placed o clinical strategies to decrease the frequency of nosocomial bacterial infections, reduce emergence of antimicrobial-resistant pathogens, and rapidly detect infection and resistance in the ICU setting. The inclusion of a reserve fund for orphan studies will enable the group to conduct innovative and public health-oriented clinical studies independent of industry funding and support. An external consultative group has been established to review the scientific agenda and comment upon study concepts. BAMSG held its first annual meeting on September 6-7, 2001, and the next meeting is scheduled for August 28-29, 2002.	Two concepts are under review for the healthcare-associated resistant bacterial infections risk group: 1) Infection control strategies to reduce colonization and infection caused by antimicrobial-resistant bacteria in adult and pediatric intensive care units with the objective of determining the effectiveness hand hygiene vs. combined infection control strategies, including screening and barrier precautions on incidence of colonization with resistant bacteria, 2) chlorhexidine-silver-sulfadiazine impregnated multilumen (CVC) vs. minocycline rifampin-coated CVC vs. standard non-medicated CVC intervention with the objectives of assessing the impact of use on blood-stream infections, the impact for prevention of colonization of CVC in young children, and the development of antimicrobial and antiseptic resistance among infecting and colonizing bacteria.
NIH	Bacteriology and Mycology Biostatistical and Operations Unit (BAMBU)	This contract supports study planning, protocol design, development, implementation, training, safety monitoring, da management and analysis, site monitoring, manuscript preparation, and other necessary and regulatory activities of clinical trials conducted through the BAMSG (see item above contract.	Awarded contract to Rho Federal Systems Division, Inc., in March 2001.
NIH	Vaccine and Treatment Evaluation Units (VTEUs)	The VTEUs are a network of 6 university research hospitals across the United States that conduct Phase I, II, and III clinical trials to test and evaluate vaccine candidates for infectious diseases. Through these sites, researchers can quickly carry out safety and efficacy studies of promising vaccines in children, adult, and specific high-risk populations. The results of these trials may have a profound effect on public health here and abroad. Through numerous studies at the VTEUs, researchers have tested and advanced vaccines for malaria, tuberculosis, pneumonia, cholera, and whooping cough. In the last 6 years alone, NIAID has supported more than 110 clinical trials through the VTEUs.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Prevention of group B streptococcal (GBS) disease contract	NIAID continues to support research on the epidemiology of GBS disease, basic biology of GBS and group A streptococci, GBS vaccine research and clinical trials of GBS conjugate vaccines through a 5-year multidisciplinary contra awarded in late 1997 to the Channing Laboratory, Brigham and Women's Hospital, Boston.	Issued a Request for Proposals to recompete this contract, entitled "Prevention of Ggoup B streptococcal disease" (AI02-13) in FY 2001; awards will be made in FY 2002.
NIH, NIAID	Division of AIDS Clinical Trials	Therapeutic clinical trials in HIV-infected populations supported by the Division of AIDS include the following: J. Coberly, Johns Hopkins University, "Efficacy of TB Chemoprophylaxis in PPD (-) HIV (+) Adults in Haiti." R. Semba, Johns Hopkins University, "Adjunct Vitamin Therapy for Tuberculosis and HIV/AIDS in Malawi." F. von Reyn, Dartmouth-Hitchcock Medical Center, "Disseminated Tuberculosis in HIV infection: Epidemiology and Prevention" in Tanzania. C. Whalen, Case Western Reserve University, "Impact of Tuberculosis on HIV Infections in Uganda – Adjunctive Prednisolone Therapy." R. Chaisson, Johns Hopkins University, "Novel TB Prevention Regimens for HIV-Infected Adults" in South Africa.	Ongoing.
**** TOP PRIORITY **** **Action Item #76: Identify, Develop, Test, and Evaluate New Rapid Diagnostic Methods for Human and Veterinary Uses with Partners, Including Academia and the Private Sector. Such methods Should Be Accurate, Affordable, and Easily Implemented in Routine Clinical Settings.**			
CDC	*C. trachomatis* resistance	*Chlamydia trachomatis* causes a sexually transmitted infection in an estimated 3 million Americans annually; untreated women can develop pelvic inflammatory disease, which can lead to chronic pelvic pain, infertility, and potentia fatal ectopic pregnancy. Several methodologies are used to assess antimicrobial susceptibility among *C. trachomatis* isolates, and this project will compare those that are currently used in an attempt to develop a standardized/reproducible assay that can be utilized for monitoring treatment efficacy.	Ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
DoD	Evaluation of commercial rapid diagnostic tests for influenza	Military populations are prone to outbreaks of febrile respiratory disease. It is expected that the use of rapid diagnostic tests for determining influenza as the cause of these outbreaks will aid in reducing unnecessary antimicrobial usage and hence help slow the emergence of AR in respiratory pathogens of bacterial origin. Two rapid diagnostic tests were evaluated against viral cultures betwee 1999 and 2001. Results showed a respective sensitivity and specificity of 100% and 63% for one test and 61% and 93% for the other. 1 of the evaluated rapid tests may be useful in respiratory disease outbreaks, but was not considered suitable for diagnoses in individual patients.	Study completed. Provided individual and summary results to the military treatment facilities providing specimens and presented them at a national meeting. Follow-up study Winter 2001 and 2002.
FDA	Test kit evaluation	Work to develop streamlined mechanisms for evaluating rap diagnostic test kits for identifying microbes and for determining susceptibility to treatments. Work with academia and industry to produce guidance documents and reference methods that could be used in evaluating new rapid diagnostics for use in the clinical setting.	1) CDRH approved a whole blood IFN-gamma assay as an aid in detection *M. tuberculosis* infection. CDC funded studies to support clinical performance of the assay in a collaborative effort with the manufacturer. Walter Reed Army Insititue of Research also provided resources for additional evaluations. 2) Completed classification for devices intended to determine resistance and susceptibility to bacterial pathogens in a shortened incubation time period; this should simplify industry's administrative submittal process. 3) Will soon publish the special control guidance document for antimicrobial susceptibility test systems. This will provide to industry the necessary elements for data gathering and presentation for a more efficient and timely review of these products. 4) Participate with NCCLS working group (including CDC and USARIMID) to establish a reference method for determining the antimicrobial susceptibility profile of Bacillus anthracis, with plans to include Yersinia pestis in the future.
FDA	Rapid diagnostic methods	Research: rapid diagnostic methods for detecting drug resistance among mycobacteria.	Collaborating with CDRH to detect drug-resistance genes in microarray.
FDA	New rapid diagnostic methods	Research: new rapid diagnostic methods for bacterials contamination of foods.	Collaborating with CFSAN research. Developed new detection method using antibodies attached to chip. Working to establish limits of detection and apply to variety of foodborne agents.
FDA	N/A	Coordinate surveillance activities with CDC.	Held initial meeting with CDC April 25, 2001; further discussions ongoing.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
USDA	Development of a rapid, sensitive and specific PCR-based test for detecting multiple antibiotic resistant Salmonella typhimurium DT104 (DT104).	ARS developed this test to provide the basis for rapid pre- and/or post-harvest detection of an important foodborne pathogen. The implementation of this test will reduce the time needed to detect DT104 from 24- 48 hours to 8-12 hours. That is, potentially contaminated meat could be detected before leaving the slaughterhouse. This system was combined with a similar test for E. coli O157:H7 so that both pathogens could be detected simultaneously.	Ongoing: USDA-ARS: Ames, IA - National Animal Disease Center (NADC).
USDA	Determination of the virulence of *Enterococci* bacteria	ARS scientists developed a multi-plex PCR for Enterococci. This assay enabled scientists to rapidly identify and differentiate Enterococcal strains which have the potential to cause disease. Unlike current methods which are time consuming, inaccurate, and costly, this PCR assay is rapid, accurate and cost-effective.	Ongoing: USDA-ARS: Athens, GA.
USDA	New methods for the determination of AR in *Campylobacter*	Antimicrobial test methodologies for *Campylobacter* are technically difficult, costly and often difficult to compare to agar dilution which is considered the 'gold standard'. A microbroth dilution assay has been developed which is cost effective, comparable to existing methodologies, easier than the agar dilution, and compatible with current equipment to determine antimicrobial susceptibility in *Campylobacter* species. This work will be presented to the National Committee for Clinical Laboratory Standards (NCCLS) for adoption as a recommended testing methodology. NCCLS determines the most accurate means of antimicrobial susceptibility testing and disseminates this information worldwide.	Ongoing: USDA-ARS: Athens, GA.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TO PRIORITY **** **Action Item #77: Encourage Basic and Clinical Research in Support of the Development and Appropriate Use of Vaccines in Human and Veterinary Medicine in Partnership with Academia and the Private Sector.**			
CDC	Measuring the effectiveness of pneumococcal conjugate vaccine for children: assessing the impact on drug-resistant Streptococcus*pneumoniae* (DRSP)	A 7-valent conjugate vaccine for *Streptococcus pneumoniae*, licensed by the FDA in 2000, is recommended by the Advisory Committee on Immunization Practices for children <5 years. Three CDC projects assess the effectiveness of this vaccine in preventing pneumococcal infections, including drug-resistant infections: 1) a case-control study of vaccine effectiveness in preventing invasive infections in children in 9 Emerging Infections Program areas in which population-based active surveillance is conducted; 2) an assessment of the impact on nasal colonization of children living in Anchorage, Alaska through annual culture surveys; 3) a community wide study of colonization in remote Alaska villages before and after introduction of the vaccine to assess the impact of the vaccine on carriage of drug-resistant strains among vaccinees and nonvaccinees. Data from these studie will be used to evaluate vaccine recommendations in the U.S Decision makers in other countries will use these data to determine whether pneumococcal conjugate vaccine should be used.	Ongoing; data collection in progress.
DoD	Double-blind placebo-controlled clinical effectiveness trial of the 23-valent pneumococcal vaccine	*S. pneumoniae* is a leading cause of morbidity in the U.S., causing an estimated 500,000 cases of pneumonia, 3,000 cases of meningitis, 50,000 cases of bacteremia, and 7,000,000 cases of otitis media annually. Navy data from 1981 to 1991 suggest that *S. pneumoniae* causes approximately 12% of pneumonia hospitalizations in the military or 9.5 admissions per 100,000 person-years. A double-blind placebo- controlled effectiveness trial of a 23-valent pneumococcal vaccine is being conducted at military training facilities. This vaccine provides coverage for 85 - 90% of the serotypes causing bacteremia in the general population, but its clinical benefit needs to be more fully characterized before the impact of its use on the emergence or spread of *S. pneumoniae* resistance can be determined.	Ongoing. Results are available to the military training facilities and are being presented at national meetings and in publications.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
FDA	Vaccine research	Research in support of the development and appropriate use of vaccines in humans to: 1) prevent viral infections, i.e. influenza, RSV; 2) prevent common bacterial infections i.e*S. pneumoniae*, non-typable*Haemophilus influenzae*, group B streptococcus, *N. gonorrhoea*, *N. meningitidis*.	12 ongoing research projects support development of vaccine for the organisms listed: 1) Completed study of protective levels of antibody against neonatal type 1a group B streptococcal infection (funded through interagency agreement with NICHD). 2) Ongoing research regarding correlates of protection against other common types of group B streptococcus. 3) Investigating correlates of protection against infection with *Streptococcus pneumonia*. 4) *N. gonorrhoeae.* Studying immunogenicity and pathogenicity of associated proteins, funded thorugh the FDA Office of Women's Health.
FDA	Vaccine development	Research in support of the development of vaccines to prevent colonization, infection, and transmission of tuberculosis	Five current projects (2 on temporary funding) that investigate vaccine candidates in mouse model with evidence of protection: combination DNA vaccine attenuated live vaccines and subunit vaccines. Grant approved to evaluate DNA vaccine in NIAID-supported guinea pig model.
FDA	Multidrug resistant TB	Research: mechanisms of resistance in multidrug- resistant tuberculosis.	Identified genetic mechanisms for multiple mechanisms of drug resistance in*M. tuberculosis.*
FDA	Drug therapy	Research: novel targets for drug therapy (to avoid resistance).	Two ongoing projects that examine the mechanisms of development of HIV drug resistance.
NIH	Phase 1 safety trial of a group B streptococcal type V polysaccharide-tetanus toxoid conjugate vaccine in healthy adults	NIAID is the sponsor of a Phase 1 safety trial of a group B streptococcal type V polysaccharide-tetanus toxoid conjugate vaccine in healthy adults. The vaccine was well tolerated in all volunteers.	Awaits funding.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Phase 1 safety trial of a group A streptococcal vaccine	NIAID is the sponsor of a Phase 1 safety trial of a group A streptococcal vaccine consisting of a live oral commensal bacterium, *Streptococcus gordonii* SP204(1-1*)* that will serve as a vector for a conserved region of the M6 protein of *Streptococcus pyogenes*. At University of Maryland's Center for Vaccine Development (a Vaccine and Treatment Evaluation Unit under contract with DMID/NIAID), a clinical trial has been completed with the vector.*S. gordonii* SP204(1-1) was implanted in healthy adults via the oral and nasal routes and found to colonize all volunteers. The vector strain was well tolerated and was successfully eradicated (spontaneously or following treatment with azithromycin).	Will conduct a phase 1 safety trial of the vaccine strain following FDA review of the data from the completed clinical trial with the vector strain.
NIH	Hexavalent group A streptococcal vaccine evaluation	NIAID is the IND sponsor for a safety and immunogenicity clinical trial to evaluate a hexavalent group A streptococcal vaccine consisting of a recombinant fusion protein containing the amino-terminal M protein fragments from 6 serotypes.	Conducting a phase 1 clinical trial at the University of Maryland's Center for Vaccine Development.
NIH	Scientific Advance: Potential of group B streptococcal (GBS) surface antigen as a vaccine candidate and/or carrier protein	Streptococcal C5a peptidase (SCPB) is a surface protein produced by all GBS serotypes, and thus this conserved protein could serve as the basis of a potential vaccine candidate and/or protein carrier that might protect against all serotypes. NIAID investigators have demonstrated that a vaccine candidate consisting of GBS III PS and SCPB resulted in an improved host immune response compared with that of other GBS III-protein conjugates. In addition, exposure of GBS to anti-SCPB antibody promoted rapid killing of the GBS, irrespective of its serotype. Studies are in progress to test whether vaccination with SCPB protects mice against GBS challenge. This new type of GBS vaccine candidate has potential to protect against a broad range of GBS simultaneously and may be more effective in preventing disease than previous GBS vaccine candidates.	Cheng Q, Carlson B, Pillai S, Eby R, Edwards L, Olmsted SB and Cleary P: Antibody against surface-bound C5a peptidase is opsonic and initiates macrophage killing of Group B streptococci. Infection and Immunity 69: 2302-2308, 2001. Grant #: R01AI20016. Principal Investigator: Patrick Cleary. Institution: University of Minnesota, Minneapolis.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Complement degrading proteins i *Streptococcus pneumoniae*	Scientists are exploring whether proteins displayed on the surface of all pneumococci, regardless of serotype, present an alternative to the current vaccine strategy. Recently, scientists found that 2 surface proteins (CppA and PhpA) are commonly present in almost all strains of *Streptococcus pneumoniae* isolated from patients.	Zhang Y, Msai AW, Baniak V, Mountzouros K, Hostetter MK, and Green BA: Recombinant PhpA protein, a unique histidine-motif containin protein from *Streptococcus pneumoniae* protects mice from pneumococcal challenge. Infec. Immunity. 69: 3827-3836, 2001. Grant #: R01AI24162. Principal Investigator: Margaret Hostetter. Institution: Yale University.
NIH	Scientific Advance: The importance of PspA as a protective immunogen	Pneumococcal surface protein (PspA), a cross-reactive protein expressed by all pneumococci, is known to elicit an antibody in animals that can passively protect mice from infection with *Streptococcus pneumoniae.* A phase I trial with recombinant PspA showed the protein to be immunogenic in humans. Pre- and post-immune serum samples from this trial were examined, and human antibody to PspA were found to protect mice from pneumococcal infection. This finding has been very important in encouraging the continued development of PspA to prevent pneumococcal infections in humans. In a related study, another group of investigators determined that there are 2 major families of PspAs that comprise over 98% of pneumococci. Their data show that vaccination with a member of 1 PspA family protects against pneumococci expressing PspA from either of these 2 families. These findings suggest that PspA may have efficacy as a human vaccine.	Briles DE, Hollingshead SK, King J, Swift A, Braun PA, Park MK, Ferguson LM, Nahm MN, Nabors G. Immunization of humans with rPspA elicits antibodies, which passively protect mice from fatal infection with *Streptococcus pneumoniae* bearing heterologous PspA. J. Infect. Dis. 182: 1694-1701, 2000. Grant #: R01AI21548. Principal Investigator: David Briles. Institution: University of Alabama, Birmingham.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Use of oral live vectors to prevent infectious diseases.	Dr. Myron Levine and his colleagues are developing an oral vaccine candidate to prevent diphtheria, tetanus (lockjaw) ar pertussis (whooping cough), which is based on the use of live, weakened strains of *Salmonella typhi* (the bacteria that causes typhoid fever). This strain has been genetically engineered to produce protective proteins from the bacteria that cause diphtheria, tetanus and pertussis. Development of an oral tetanus vaccine represents the initial step in this process. In a "proof-of-principle" (Phase 1) clinical trial, Dr. Levine's laboratory has recently shown that a single oral dose of such an engineered S. typhi-based tetanus vaccine can stimulate the appearance of protective antibodies (42 times above the level known to be protective!) in an individual who lacked tetanus antibodies prior to vaccination.	Tacket CO, Galen J, Sztein MB, Losonsky G, Wyant TL, Nataro J, Wasserman SS, Edelman R, Chatfield S, Dougan G, Levine MM: Safety and Immune Responses to Attenuated Salmonella enterica Serovar Typhi Oral Live Vector Vaccines Expressing Tetanus Toxin Fragment C. Clinical Immunology 97:146-53, 2000. Grant #: R01 AI29471. Principal Investigator: Myron Levine. Institution: University of Maryland School of Medicine
NIH	Scientific Advance: Use of molecular analysis to define the human antibody repertoire specific for polysaccharide antigens of the pneumococcal bacteria.	Work by Dr. Donald Reason and his colleagues has revealed that the 23F capsular polysaccharide from the *Streptococcus pneumoniae* organism presents at least 2 different surface markers/determinants to the human immune system, and the response for each of these markers (i.e., antigens) is dominated by antibodies derived from a highly restricted set of genes. Findings indicate that, a successful response to important bacterial antigens is dependent on a very restricted set of genetic elements. The absence of these genetic elements could result in very specific defects in the immune repertoire that would leave the individual at-risk for infection with that specific strain of bacteria. Continued research in this area will provide a detailed understanding of the molecular determinants of pneumococcal immunity in human, and may help identify strategies that would facilitate the development of more efficacious vaccines.	Lucas, AH, Moulton, KD, Tang, VR, and Reason, DC: Combinatorial library cloning of human antibodies to *Streptococcus pneumoniae* capsular polysaccharides. Variable region primary structures and evidence for somatic mutation of Fab fragments specific for capsular serotypes 6B, 14, and 23F. Infection and Immunity 69:853-64, 2001. Investigator: Alexander Lucas. Institution : Children's Hospital Oakland Research Institute. Grant # : R01 AI25008.
NIH	Vaccine Action Program	The INDO-US Vaccine Action Program initiated in 1987 is a bilateral program that focuses on the development of safe ar effective vaccines for major communicable diseases of interest to the 2 countries through joint research and development efforts.	Currently, the focus of the program is on HIV/AIDS, malaria, and tuberculosis.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Adult efficacy trial using acellular pertussis vaccine	An adult efficacy trial using acellular pertussis vaccine was recently completed in 2,784 subjects 15-65 years of age to define the incidence, clinical spectrum, and epidemiology of pertussis infection and disease in adolescents and adults as well as define the safety, immunogenicity, and efficacy of an acellular pertussis vaccine designed for use in older individuals. The acellular vaccine was shown to be safe with no vaccine associated serious adverse events. Confirmed pertussis occurred in 2 vaccines and 9 controls, yielding an efficacy of 77%. This estimate of efficacy is similar to that observed in young children.	These data suggests that an acellular pertussis vaccine given to adolescents and adults in the form of a dTaP booster would be safe and effective in reducing the burden of disease in this population in addition to reducing secondary transmission to infants.
NIH, USAID	Randomized, double-blinded, controlled Phase III efficacy trial of pneumococcal conjugate vaccine	NIAID is conducting a randomized, double-blind, controlled Phase III efficacy trial in The Gambia, West Africa, using a 9-valent pneumococcal conjugate vaccine manufactured by Wyeth-Lederle Vaccines and Pediatrics (WLVP). The trial is designed to determine the impact of the pneumococcal conjugate vaccine, when administered with DPT/Hib (TetramuneTM) in the same syringe, on childhood mortality due to invasive pneumococcal disease. The main endpoint will be overall mortality; however, secondary endpoints will include the effect of the vaccine on mortality from ALRI and on invasive pneumococcal disease caused by pneumococci of vaccine serotype. Approximately 45,000 children will be recruited into the trial from shortly after birth over a period of and a half years. Three doses of the DTP/Hib vaccine mixed with the 9-valent pneumococcal conjugate vaccine will be administered to half the children at 2, 3, and 4 months of age The other half will receive just the DTP/Hib vaccine.	Initiated, phase III trial. It is anticipated that the trial will last a period of 5 years.
NIH	Prevnar study in Navajo and Apache populations	A successful Phase III pneumococcal conjugate efficacy trial in the Northern California Kaiser Permanente health care system subsequently led to licensure of the WLVP vaccine for infants up to 24 months of age in March 2000. A second vaccine efficacy trial was completed in a Navajo/Apache population in the Southwest U.S.	The newly licensed pneumococcal conjugate vaccine (Prevnar) has been found to be efficacious in protecting against invasive pneumococcal disease as well as protecting vaccinated children from becoming carriers to the 7 serotypes of *Streptococcus pneumoniae* associated with the vaccine.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Prospective, randomized, double-blinded, controlled, multisite trial of acellular pertussis vaccine in healthy adults and adolescents	NIAID recently completed a prospective, randomized, double-blinded, controlled, multisite trial to evaluate the protective efficacy of an acellular pertussis vaccine in 2,700 healthy adolescents and adults. Enrollment of the subjects was conducted at several NIH-sponsored VTEUs and at other contract institutions.	An analysis of study findings showed that the acellular vaccine was safe in this population.
NIH	Respiratory syaacytial virus (RSV) vaccine trial in healthy third-trimester pregnant women	NIAID is the sponsor of a randomized, double-blinded, placebo controlled, Phase 1 safety trial at Baylor College, utilizing an RSV subunit vaccine in healthy third-trimester pregnant women. All enrolled subjects were vaccinated and delivered healthy babies (last clinical observations were in May 2001).	Sample collection and analysis is ongoing.
NIH	Scientific Advance: Potential novel, vaccine candidates against bacterial meningitis identified from genomic sequences	*N meningitidis* is an important cause of bacterial meningitis and is on the increase in the U.S. Dr. Stojiljkovic and his colleagues conducted a computer search of *N. meningitidis* and *N. gonorrhoeae* genome databases to identify new outer membrane proteins (OMPs) of the bacteria and subsequently characterized the proteins and determined their distribution on the bacterial surface. Previous studies established that this family of OMPs function as channels to allow access to nutrients and to obtain iron from the environment. In the current study, 3 proteins designated F, G, and H were identified. One of these, protein H, is expressed in all strains of *N. meningitidis* examined and is exposed on the surface of the bacteria. Protein H is also *expressed in N. gonorrhoeae but not in commensal Neisseria* and may play a role in the disease process. Future efforts will determine its usefulness as a vaccine candidate.	Turner PC, Thomas CE, Stojiljkovic I, Elkins C, Kizel G, Ala'Aldeen DA, Sparling PF. Neisserial TonB-dependent outer-membrane proteins: detection, regulation and distribution of three putative candidates identified from the genome sequences. Microbiology 47: 1277-90, 2001. Grant #: RO1AI42870. Principal Investigator: Igor Stojiljkovic. Institution: Emory University School of Medicine, Atlanta, GA

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Scientific Advance: Vaccination with genetic material coding for *Mycobacterium tuberculosis*	(Mtb) specific proteins provides protection similar to bacillus calmette guérin in mouse models. One approach to developing a badly needed TB vaccine is to identify proteins from Mtb, and use their genetic material, rather than the proteins themselves, to vaccinate animals against TB. Dr. Yasir Skeiky and colleagues used a special technique to isolate mouse immune cells and tested a series of Mtb proteins to identify those proteins that produced a response by the isolated immune cells. The researchers then cloned the genetic information for these proteins and used it to vaccinate mice. These investigators were successful in demonstrating that in 1 case, vaccination with genetic material was as effective in protecting the animals against TB as was vaccination with live BCG.	Skeiky YAW, Ovendale PJ, Jen S, Alderson MR, Dillon DC, Smith S, Wilson CB, Orme IM, Reed SG, Campos-Neto A: T cell expression cloning of a *Mycobacterium tuberculosis* gene encoding a protective antigen associated with the early control of infection. Journal of Immunology.165:7140-7149, 2000. Grant #s: R01 AI43528; R01 AI45707; R01 AI44373 Principal Investigators: Antonio Campos-Neto; Ian M. Orme; Steven G. Reed. Institutions: Infectious Diseases Research Institute; Colorado State University; Infectious Diseases Research Institute.
NIH	Scientific Advance: Engineered *bacillus calmette* guérin vaccine strain provides protection against TB in animal models	Bacillus calmette-guérin (BCG) is used as a vaccine against TB, but provides varying degrees of protection. One strategy researchers are using to improve BCG is to engineer this bacterium to produce Mtb-derived proteins in the hope that the immune system will then be able to respond more efficiently to Mtb infections. Dr. Marcus Horwitz and colleagues used this approach to construct a BCG strain that produces an Mtb protein, the 30-kDa major secretory protein. Guinea pigs vaccinated with this modified BCG were protected from TB to a larger degree than animals vaccinated with the unmodified BCG. This demonstrates that the existing vaccine against TB, BCG, can potentially be improved by engineering it to produce Mtb specific proteins	Horwitz M, Harth G, Dillon MJ, Masleša-Galić S: Recombinant bacillus Calmette-Guérin (BCG) vaccines expressing the *Mycobacterium tuberculosis* 30-kDa major secretory protein induce greater protective immunity against tuberculosis than conventional BCG vaccines in a highly susceptible animal model. Proceedings of the National Academy of Sciences USA 97:13853-13858, 2000. Grant #: R01 AI31338. Principal Investigator: Marcus Horwitz. Institution: University of California Los Angeles, CA.
NIH	Contribution of CD8+ T-cells to the destruction of *Mycobacterium tuberculosis* in the host	Research carried out under Dr. Sungae Cho and colleagues showed that a subset of these specialized immune cells, called CD8+ T cells, can contribute to this host defense and mediate the destruction of the infected host cells. Previously the role of this CD8+ T subset in the immune response to Mtb infection had been unclear. This finding may lead to new therapeutic and preventive approaches for TB.	Cho S, Mehra V, Thoma-Uszynski S, Stenger S, Serbina N, Mazzaccaro RJ, Flynn JL, Barnes PF, Southwood S, Celis E, Bloom BR, Modlin RL, Sette A: Antimicrobial activity of MHC class I-restricted CD8+ T cells in human TB. Proceedings of the National Academy of Sciences USA 97 (22):12210-12215, 2000.
NIH	Application of data on human major histocompatibility complex molecules to the improvement of vaccines.	A contract awarded in FY 1999 “High Throughput Identification of Broadly-Reactive HLA-Restricted T Cell Epitopes” (Dr. Alessandro Sette, Epimmune Corp.) has defined a large number of short protein fragments from Mtb that are candidate immunogens for diverse human populations.	Ongoing. Results are available to the military training facilities and are being presented at national meetings and in publications.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #78: Encourage Basic and Clinical Research in Support of Novel Approaches to Preventing or Treating Infections with Resistant Organisms That Occur in Humans and Animals by Partnering with Academia and the Private Sector.			
FDA	Guidance document	Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals	Working group formed; Draft document completed.
NIH	Partnerships for novel therapeutic, diagnostic and vector control strategies in infectious diseases program announcement (Also applicable under #76 and #77)	Special initiative of NIAID to support the development of drugs and diagnostics for human infectious diseases that cause a significant public health burden but are not a current priority for industry. Focus includes development of agents t address infections for which drug resistance is making current therapies ineffective.	Released December 4, 2001.
NIH	Challenge Grants	Through a special appropriation from Congress, a new government/industry partnership was set up with industry matching NIAID funds 1:1, using milestone-driven goals for evaluation and allowing substantive involvement on the part of NIH in drug and vaccine development projects.	Three TB challenge grants were awarded to the following investigators in September 2000: 1) Marina Protopopova (Sequella, Inc.) to develop a new generation of ethambutol derivatives for TB treatment. 2) John Lonsdale (GlaxoSmithKline) to develop advanced thiolactomycin based drug candidates against TB and Gram-positive and Gram-negative bacterial infections. 3) Steven Reed (Corixa Corp.) to conduct preclinical testing of new TB candidate vaccines.
NIH, NSF, USDA	International Cooperative Biodiversity Groups Progra (ICBG)	International Cooperative Biodiversity Groups Program (ICBG)	Currently 6 awards have been made to multidisciplinary research groups that also include in-country, research-capacity strengthening activities, community education programs, ethnobotanically-based plant collections, and partnerships with a pharmaceutical company. ICBG investigators have achieved extensive progress identifying bioactive compounds from plants of Central and South America, Nigeria, Cameroon, Madagascar, Laos, and Viet Nam.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
CDC, NIH, USAID	Global Alliance for TB Drug Development (GATB)	The GATB is a new public/private partnership to stimulate new drug development against tuberculosis. NIAID is involved in this collaboration with private partners, who are contributing to the development of new drugs to shorten the treatment of TB and facilitate its control in the poorest countries. Over 30 organizations are stakeholders in this innovative public-private partnership, including the Bill & Melinda Gates Foundation, CDC, NIAID/NIH, Rockefeller Foundation, USAID, the World Bank, and WHO. For a comprehensive list, see http://www.tballiance.org	NIAID staff assisted the GATB in developing a process for soliciting requests for drug discovery and development proposals from the global research and development community and in the scientific peer review of the proposals. Of the 107 proposals received, 11 were identified for potential support by the GATB as preclinical candidate compounds or as clinical trials of new drug regimens.
NIH	Pharmaco-economics report on TB drug development	Through participation in the GATB, many NIAID-supported investigators and staff contributed to a publication detailing the investments and potential markets required to develop a new drug for the treatment of TB. The NIAID TB Technology Transfer contractor (Research Triangle Institute of North Carolina) organized, researched, coordinated, and edited a major report on the economic factors involved in bringing a new anti-tuberculosis drug to market. This report will be a rigorous, authoritative source of information on the epidemiology of TB, potential market for new anti-TB drugs, cost of TB drug development, and options for funding and conducting drug development. The report will provide data required for informed investment decisions by industry, foundations, government organizations, and world health and financial organizations.	To be published by the GATB.
NIH	Tuberculosis Antimicrobial Acquisition and Coordinating Facility (TAACF)	New drugs to treat TB are being screened through this NIAID contract. Southern Research Institute in Birmingham, Alabama has established a facility to acquire compounds for screening against Mtb, maintain a computerized chemical database of compound structures, coordinate and distribute compounds for evaluation *in vitro* and in an animal model, and report data back to suppliers.	The TAACF has contacted over 3,500 chemists throughout the world seeking candidate anti-TB compounds. Over 55,43 compounds have been received from academic and private sector investigators, principally in the United States and Europe, with growing involvement of scientists from Africa, Asia, Australia, South America, and other geographic sites. http://www.taacf.org

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Submission of compounds for *in vitro* evaluation	Staff have selected for evaluation more than 8,000 compounds, based on their chemical structure, from the National Cancer Institute (NCI) chemical repository of over 500,000 compounds. Of these compounds, 500 have shown initial *in vitro* activity against a wild-type strain, and of these, approximately 100 have promising *in vitro* activity against isoniazid (INH)-resistant strains. A large part of this effort is conducted under an interagency agreement with the Health Resources and Services Administration at the Gillis W. Long Hansen's Disease Center. Efficacy evaluations in animal models of TB are being conducted on selected compounds.	Ongoing.
NIH	High-throughput screening contract (N01-AI-15449) with Southern Research Institute	This contract awarded to Birmingham, Alabama in response to RFP AI01-13, "Tuberculosis Drug Screening: Part B" will provide a high throughput screening capability to develop and implement biochemical, target-specific Mtb drug screening assays and to develop and implement Mtb metabolic stage-specific drug screening assays.	Ongoing.
NIH	National cooperative drug discovery groups for the treatment of opportunistic infections associated with AIDS (NCDDG-OI)	To stimulate private sector involvement in the development of drugs for the treatment of TB, three NCDDG-OI's (P. Brennan, Colorado State University; L. Heifets, National Jewish Center; W. Jacobs, Albert Einstein University; J. Sacchettini, Texas A&M University) actively collaborated with pharmaceutical firms with an interest in TB drug development (Glaxo SmithKline). A fourth NCDDG-OI group is studying the Mtb alanin racemase for targeted drug design (Kurt Krause, University of Houston).	Collaborations ongoing.
NIH	Evaluation of the utility of lytic phages in dealing with Vancomycin Resistant Enterococci (VRE) infections: preclinical trials	A collaboration is ongoing between NIAID, through the Maryland Immunoscenescence/Immunosuppression Research Group Vaccine and Treatment Evaluation Unit, an a small biotechnology company to demonstrate in animal studies the safety and efficacy of a lytic phage preparation in reducing or eliminating VRE infections. The ultimate goal of this collaboration is to develop an effective prophylactic and therapeutic strategy for dealing with infections caused by VRE in seriously ill patients.	If animal proof of principle experiments are successful, then Phase I clinical trials will be initiated.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
NIH	Initial safety and pharmacokinetics trial of intravenous immunoglobulin with enhanced levels of antibodies to *Staphylococcus aureus* in healthy adult volunteers	A collaboration is ongoing between a small vaccine manufacturer and the NIAID through the Maryland Immunoscenescence/Immunosuppression Research Group Vaccine and Treatment Evaluation Unit, to initiate Phase I safety trials of a hyperimmunoglobulin product. The administration of human hyperimmune globulin has been shown to significantly reduce the rate of serious infection with *Hemophilus influenzae* type b, *Klebsiella*, sp., *Pseudomonas aeurginosa* and other bacterial infections. It is hoped that this therapeutic approach will ultimately be useful as adjunctive treatment with antimicrobials in seriously ill patients with *S. aureus* infections.	Protocol under review within NIAID; clinical trials are planned for the Maryland Immunoscenescence/Immunosuppression Research Group Vaccine and Treatment Evaluation Unit.
NIH	Scientific Advance: Novel approach to kill streptococcal bacteria offers hope for controlling streptococcal infections.	NIAID-supported scientists recently demonstrated that a bacteriophage (virus that infects bacteria) enzyme can kill group A streptococci (GAS) on contact. The investigators found that when a bacteriophage reproduces in a bacterial cell, the progeny bacteriophage produce enzymes called lysins that destroy the cell wall of bacteria in order to release the progeny bacteriophage. These enzymes specifically kill the bacteria in which they were produced and may represent an effective way to control GAS infections. Using a mouse model, the investigators report that this lysin enzyme was shown to prevent and eliminate colonization of the upper respiratory tract of mice by GAS. This approach has potential to reduce GAS from carriers and infected individuals, thus reducing associated disease.	Nelson D, Loomis L, and Fischetti VA: Prevention and elimination of upper respiratory colonization of mice by group A streptococci by using a bacteriophage lytic enzyme. Proceedings of the National Academy of Science USA 98: 4107-4112, 2001. Grant #: R37AI11822. Principal Investigator: Vincent A. Fischetti. Institution: Rockefeller University, New York.
Focus Area IV: Product Development			
**** TOP PRIORITY ** Action Item #79: Create An Interagency AR Product Development Working Group To Identify and Publicize Priority Health Needs in Human and Animal Medicine for New AR Products (e.g., Innovative Drugs, Targeted Spectrum Antibiotics, Point-of-Care Diagnostics, Vaccines and Other Biologics, Anti-Infective Medical Devices, and Disinfectants).**			
FDA	Interagency AR product development working group	FDA has chosen to perform these cooperative activities using existing advisory committees with other agency and industry participation.	Initial AC meeting Feb 19-20, 2002. Docket available for additional comment.

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
**** TOP PRIORITY **** **Action Item #80: Identify Ways (e.g., Financial and/or Other Incentives or Investments) To Promote the Development and/or Appropriate Use of Priority AR Products, such as Novel Compounds and Approaches, for Human And Veterinary Medicine for Which Market Incentives Are Inadequate.**			
FDA	New AR products	Identify and publicize priority public health needs for new AR products; identify the kinds of products we would want to see developed.	Preliminary meeting has occurred; working group is forming; future action TBD CDER advisory committee held February 2 2002.
FDA	Economic incentive program	Consider economic incentives for encouraging the development of medical products targeted toward resistant organisms.	Pending discussion.
FDA	Joint efficacy workshop and advisory committee meeting	Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures o efficacy.	Completed February and March 2001. Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines planned for Spring 2002.
FDA	See Action Item #79 (Interagency AR Product Development Working Group)	See Action Item #79 (Interagency AR Product Development Working Group).	See Action Item #79 (Interagency AR Product Development Working Group).
FDA	Maternal immunization	Development of approaches for licensure of vaccines to prevent group B streptococcal infections. CDC, NIH, FDA meeting May 1998 regarding Maternal Immunization and NIAID, NIH Advisory meeting regarding serological assays.	Continued regulatory and research effort to remove barriers to product development under current funding.
FDA	Guidance document	Guidance document: Biologics Derived from Bioengineered Plants for Use in Humans and Animals.	Working group formed; Draft document completed.
Action Item #81: Consider, in Consultation with Academia and Industry, Whether Government Has a Constructive Role To Play in Discovery of Drugs and Other Products Targeted To Address Areas Where Market Incentives are Limited and Unmet Needs Exist (e.g., Novel Antimicrobial Drugs Targeted To Specific Resistant Organisms).			

AGENCY	PROJECT TITLE	DESCRIPTION	STATUS
Action Item #82: Continue Ongoing Approaches that Streamline the Regulatory Process, Including Clinical Trials and Enhanced Pre-Clinical Studies (e.g., Use of Pharmacokinetics and Pharmacodynamics Data) To Help Bring AR Products (Including Drugs, Vaccines, Diagnostics and Devices) To Market as Efficiently and As Rapidly as Possible, While Still Assuring Their Safety and Efficacy.			
FDA	Workshop and committee meeting on efficacy	Identify ways to promote the development and licensure of additional pneumococcal conjugate vaccines. Joint NIAID/CBER Workshop and Vaccines and Related Products Advisory Committee addressed issues regarding measures o efficacy.	Completed February and March 2001 Workshop regarding correlates of protection for use in licensure of additional pneumococcal vaccines planned for Spring 2002.
FDA	Regulatory requirements – industry and scientific community	Clarify FDA regulatory requirements to both industry and the scientific community.	1) Down classification for devices intended to determine resistance and susceptibility to bacterial pathogens in a shortened incubation time period is completed and should simplify industry's administrative submittal process. Can be referenced to Action Item #76. 2) The special control guidance document for antimicrobial susceptibility test systems will be published soon. This will provide industry with the necessary elements for data gathering and presentation for a more efficient and timely review of these products. Can be referenced to Action Item #76 3) Presentation on regulatory requirements for tests of use in AR initiatives to the Professional IVD Roundtable (a group representing all major professional laboratory groups) on June 6, 2001. Discussion on obstacles and issues which might exist in technology transfer.
FDA	Topical micobicides	CBER/CDER working group on Topical Microbicides.	Working group formed; Draft document completed.
FDA	See Action Item #80 (Maternal Immunization).	See Action Item #80 (Maternal Immunization).	See Action Item #80 (Maternal Immunization).
FDA	See Action Item #80 (Guidance Document).	See Action Item #80 (Guidance Document).	See Action Item #80 (Guidance Document).
Action Item #83: In Consultation with Stakeholders and Expert Consultants, Identify Ways To Promote The Development of New and Alternative Veterinary Treatments and The Improved Use of Existing Therapies That Are Unlikely to Stimulate Resistance to Drugs in Human Medicine.			
FDA	GAP and GMP Development	Develop new Good Agricultural Practices and Good Manufacturing Practices based on scientific findings.	At concept stage.
Action Item #84: Strealine the Regulatory and Approval Process for Veterinary Antimicrobial Drugs and Related Products That Are Unlikely, Now or in the Future, To Result In Transfer of Antimicrobial Resistance To Humans.			